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CONCERNING THE NATURE OF "PROTOZOAN-LIKE" CELLS IN CERTAIN LESIONS OF INFANCY *

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BOSTON

The so-called "protozoan-like" cells with which this paper is concerned were first described in 1904 by Jesionek and Kiolemenoglou,[1] who found them in the kidneys, lungs and liver of an eight months fetus, in intimate association with lesions of hereditary syphilis. The authors pictured these extraordinary structures as measuring on an average from 20 to 30 microns in diameter, usually oval in outline, possessing a well defined, though not sharply stained, cuticular zone having the appearance of a capsule. The nuclei were large, eccentrically placed, each containing a very pronounced "central nuclear body" surrounded by two well defined zones, an inner dark and an outer clear zone. The entire nucleus appeared separated from the cell body by a membrane. In the clear outer zone of the nucleus were found spherical, darkly staining granules of different sizes averaging 1 micron. The width of the nucleus, inclusive of the membrane, measured 10 microns. The cell-body contained many granules, especially numerous at the pole opposite the nucleus, while nearer the nucleus were spherical vacuoles. Cells of this description were found in greatest numbers in the kidneys, occurring characteristically in groups of from ten to forty, lying in the interstitial tissue of the midzone where syphilitic inflammatory changes were most in evidence. None was observed either in glomerulus, tubule or blood vessel. In the lungs and liver similar cells were present, usually singly, at most in groups of four. Those in the lungs were situated in alveoli and bronchi, as well as in inflammatory interstitial tissue.

This publication induced Ribbert [2] shortly afterward to record observations on a similar case, also a syphilitic infant, which he had

* Received for publication, Dec. 13, 1920.

* From the Department of Pathology and Cancer Commission of Harvard University.

1. Jesionek and Kiolemenoglou: Ueber einen Befund von protozoënaritgen Gebilden in den Organen eines hereditärluetischen Fötus, München. med. Wchnschr. **43**:1905, 1904.

2. Ribbert: Ueber protozoënartige Zellen in der Niere eines syphilitischen Neugeborenen und in der Paroti von Kindern, Centralbl. f. Allg. Path. u. Path. Anat. **15**:945, 1904.

studied twenty years previously, and failing an interpretation, had put aside. In the kidneys only of this infant he found unusually large cells, which evidently corresponded to those described by the previous authors. They lay in great masses within the lumina of nearly all convoluted tubules, never outside in interstitial tissue, nor in straight tubules and glomeruli. They filled the lumen, distended it and pressed the epithelium out flat about them. Here and there the epithelial cells were pressed apart by the "foreign" cells whose protoplasm extended to the membrana propria. The large cells possessed a round or oval homogeneous nucleus with a relatively voluminous, likewise homogeneous but not in all cases visible intranuclear body. The nucleus was separated from protoplasm by a clear zone, giving an impression as if its substance had contracted from the nuclear membrane. Ribbert's sections from this case were old, not well stained, and cellular details he admits were not so clear as might have been wished. In the same paper, he mentions two instances in which he found similar cells in the parotid gland of infants, one 3 months, the other 1 year of age. In these two there was no suspicion of syphilis. Only the parotid glands were studied, and in them characteristic large cells occurred only within ducts, singly or in groups.

In 1910 Smith and Weidman [3] discovered similar large cells in a stillborn fetus. The infant was not syphilitic and weighed seven and one-half pounds. The cells were present in sections of lung, liver and kidney, and not associated with any observed lesion, except minute foci of lymphocytes and polymorphonuclear leukocytes in the renal cortex and liver. The large cells were in groups in the kidney, always in renal tubules, either within or without inflammatory foci. In the liver one such cell was seen within an inflammatory focus. In the lung no inflammatory process was observed, but a number of separate large cells were found always within alveoli.

In 1915, these authors recorded a second case in which cells of the same character were present in an infant 2 months of age, regarded clinically as syphilitic, though this diagnosis was not confirmed by history nor by a positive Wassermann test. The infant died of a subacute organizing bronchopneumonia, and the large cells were observed only in the lungs. They were scattered among cells of inflammatory origin, never aggregated, and occurred only sparsely distributed throughout the section. There was a chronic interstitial pancreatitis, but no similar cells were seen in this organ.

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3. Smith, A. J., and Weidman, F. D.: Infection of a Still-Born Infant by an Amebiform Protozoan (Entameba Mortinatalium, n. s.), Univ. Penn. Med. Bull. **23**:285, 1910. Further Note on the Occurrence of Entamoeba Mortinatalium as a Human Parasite, Am. J. Tropical Dis. & Prev. Med. **2**:256, 1914.

The above records are the only observations on these peculiar structures in human pathology which we have been able to find in the literature, and each observer has regarded them as possibly protozoan in nature. Smith and Weidman definitely classify the cells as endamebas and have given them the name *Endamoeba mortinatalium*. It would seem almost incredible that the condition could be one of protozoan infection confined to fetal and infantile life, and yet the large cells have appeared so unlike any tissue cell that previous observers have leaned toward this rather improbable interpretation. In none of the above instances has any evidence been presented of a possible histogenous origin. Jesionek and Kiolemenoglou submitted their preparations to the eminent protozoölogist Richard Hertwig, who thought the structures might represent a kind of gregarine. Ribbert sought the opinion of the biologists, Ehlers and Rhumbler, who would not commit themselves definitely, but stated that no morphologic criteria were absolutely against the protozoan character of the cells. Smith and Weidman state "it cannot be seriously thought that these cells are other than protozoan parasites" and proceed to classify them as *Endamoeba mortinatalium*.

The case which we shall describe is of especial interest in that it furnishes definite evidence of the histogenous origin of these cells, shows their transportation through the blood stream, and indicates that this peculiar cellular change is a retrogressive one by which certain cells become independent of the body tissues and capable perhaps of wandering about exhibiting a certain similarity to protozoa.

REPORT OF CASE

History.—C. D., was first seen Nov. 6, 1919, at the age of 6 weeks. Two children had previously died at about the age of 3 months of a disease which the mother says was similar to the present trouble. One child, aged 2 years, is strong.

Fourth pregnancy, full term, birth weight 9 pounds. Always breast fed. Thighs were raw at three weeks but healed up rapidly with white ointment. Ever since birth has had green stools. Day before coming in feet swelled up. During the past two days the child has had no appetite. Nurses normally but acts now and then as if there was considerable mucus in throat.

Physical Examination.—His physical examination showed a fat, pale baby, which looked puffy. Anterior fontanel was open and level. Pupils were equal and reacted to light. Mouth and throat normal. There was no enlargement of peripheral lymph nodes. Heart and lungs were normal. Liver and spleen were not felt. Knee jerks equal and normal. There was no Kernig sign. Scattered over the buttocks, legs and abdomen there was a superficial rash which was characteristic of a napkin rash. The urine at this date contained a marked trace of sugar with Benedict's solution, no albumin. November 9 and 11 the urine gave a precipitate with Benedict's solution. No acetone. The stool was a characteristic one of a normal breast fed infant and contained a large excess of fat. This, however, is not abnormal.

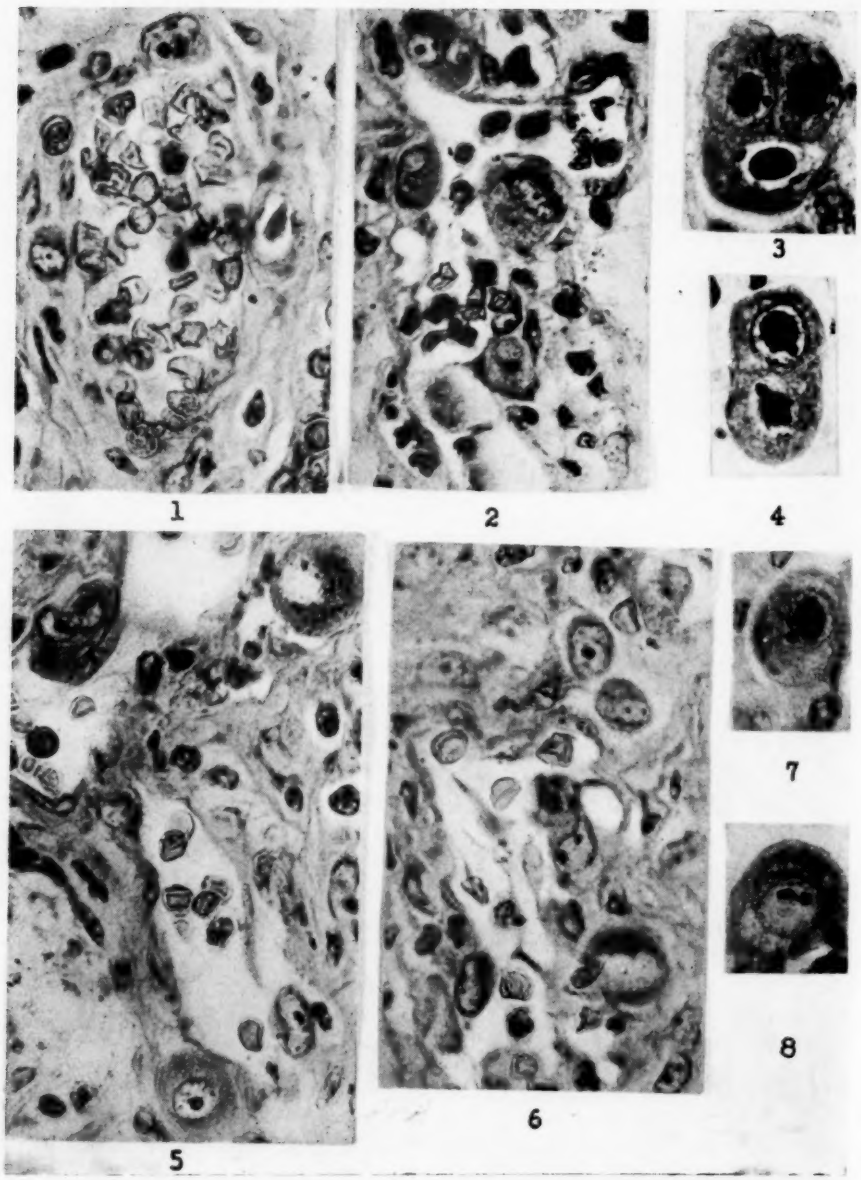


Fig. 1.—Transition forms of large cells in wall of bronchial vein. Note variation in size of dark intra-nuclear bodies. Cell in right wall has large clear nucleus, dark irregular intranuclear body. All photographs same magnification, Zeiss 2 mm. oil immersion objective, No. 2 eye-piece.

Fig. 2.—Transition forms of large cells, in wall of bronchial vein.

Fig. 3.—Group of three large cells in alveolus of lung.

Fig. 4.—Single large cell in alveolus of lung with horse-shoe shaped nucleus and intranuclear body, giving in section the appearance of double nucleus.

Fig. 5.—Transition forms of large cells in wall of bronchial vein.

Fig. 6.—Transition forms of large cells in wall of bronchial vein.

Fig. 7.—Large cell showing spherical bodies in cytoplasm.

Fig. 8.—Disintegrating form of large cell.

The analysis of the mother's milk November 13 showed: Fat, 2 per cent.; lactose, 7.2 per cent.; protein, 1.4 per cent. November 18 it was noted that the baby had been edematous, the edema extending up the legs to the abdomen.

The urine at that date showed a reduction with Benedict's solution after boiling in a water bath for five minutes. When the urine was kept for any length of time it did not show any reduction with Benedict's solution. November 19 the reduction was found again with Benedict's solution and negative with phenalhydrazin test. At no time did the urine contain acetone or diacetic acid. On this date there were many pus cells in the sediment. The renal function test (phenolphthalein) showed 35 per cent. The baby's blood sugar was 9.4 mg. per 100 c.c. of blood. The baby's blood urea N = 26 mg. per 100 c.c. of blood.

Baby died a few days later. Edema, cough and loss of appetite being the prominent features on the third to fourth day preceding death.

Wassermann reaction on mother's blood was negative.

Necropsy.—Eight hours postmortem.

External Examination: The body is that of a 2 months old white male infant. There is very marked pallor. Considerable edema of feet, legs and hands. Abdomen is greatly distended, evidently by intestinal gas. Pupils equal, mucous membranes pale. No discharge from ears or nose. No eruption present. The body is poorly nourished.

Fig. 9.—Large cell lodged in capillary of liver.
Fig. 10.—Large cell free in bronchial lumen in midst of cellular exudate.
Fig. 11.—Large cell in alveolus of lung, showing reticular cytoplasm.

Peritoneal Cavity: On opening the abdominal wall very little subcutaneous fat is found. Both small and large intestines are greatly ballooned with gas. Peritoneal surfaces are smooth, shiny, and moist. No evidence of inflammation. Organs are normally situated. The liver is very large, pale, yellow and fatty. Spleen perhaps slightly larger than normal. No marked enlargement of lymph glands. Pancreas is small, granular, firm and white. No excess of peritoneal fluid.

Thoracic Cavity: No excess of fluid in either pleural cavity. The lungs are voluminous, and both lower lobes completely consolidated. There is a little translucent, granular fibrin in places over these lobes. Pericardium is normal. Heart appears normal. Thymus small.

Lungs: Both lower lobes are quite similar in appearance. They are voluminous and completely consolidated. The margins are thin and delicately frayed, but the delicate filaments are not fibrin, being tough and adherent. The posterior portion of the apices are purplish in color, the remainder of the lobes pale grayish yellow. The pleural surfaces are smooth, and no fibrin is detected with certainty. The two upper lobes, and the middle lobe, show some pale edema posteriorly, and a few small hemorrhagic areas here and there, but no diffuse consolidation. They are air containing, and somewhat emphysematous, but no ruptures or bullae are found.

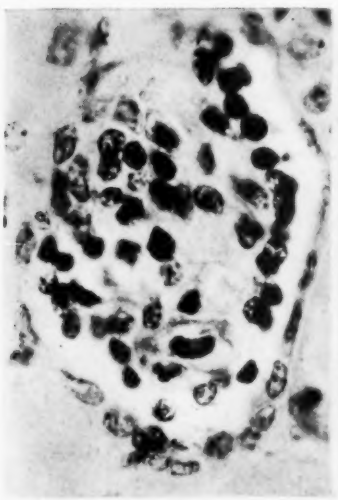
On section through the lower lobes the bronchi are seen to be dilated and filled with plugs of yellow pus. Even the smaller branches are dilated and pus-containing. The bronchial walls appear thickened. The intervening alveoli are filled with exudate and appear pale and yellowish. The entire lobe is fairly firm, but pus can be expressed with little pressure, and the gross appearance is that of a subacute confluent broncho-pneumonia, lobar in distribution, with purulent bronchitis and bronchiectasis.

Heart: Myocardium and valves appear normal.

Intestinal Tract: Stomach and intestine appear normal, except for post-mortem softening of mucosa and distention with gas. Mesenteric lymph glands not enlarged.

Spleen: Perhaps slightly larger than normal, reddish purple in color, fairly firm and malpighian bodies not especially conspicuous.

Liver: Very much enlarged, capsule tense and smooth, pale and yellow. Cut surface greasy; lobulation rather indistinct; cut surface uniform. Appearance is that of very marked fatty change. Gallbladder and ducts appear normal.



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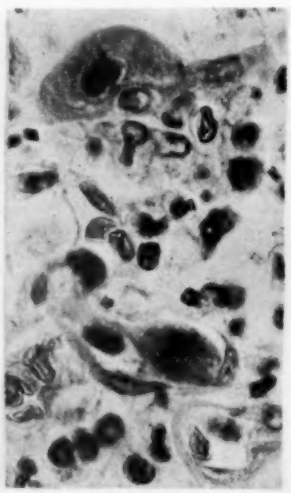

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Fig. 12.—Large cell lodged in capillary of renal glomerular tuft. The cell is situated at lower pole of tuft and shows well the clear nuclear space and dark oblong intranuclear body.

Fig. 13.—Large cell filling capillary of lung alveolus (lower). Upper, large cell partially lines alveolar wall.

Fig. 14.—Two large cells free within vein of bronchial wall.

Pancreas: Is small, white, firm and granular. There appears to be a diffuse increase of interlobular, and interacinar connective tissue and atrophy of parenchyma. Ducts not dissected out.

Kidneys: Appear larger than normal, pale and moist. Capsule strips easily and leaves a smooth, pale uniform surface. Cut surface shows a thickened cortex, somewhat more opaque than normal, but with regular striations and architecture.

Suprarenals: Appear normal in gross.

Urinary Bladder: Contains clear urine, about 50 c.c. in amount. The pelvic organs show no obvious pathological change in gross.

Microscopic Examination. — The pancreas microscopically shows fibrosis and dilatation of ducts. Numerous islands are found and they appear normal. Glycogen is not present in the liver, but occurs in considerable quantity in the ascending loops of Henle in the kidneys.

Stained sections of heart, lungs, liver, pancreas, kidneys and suprarenals by Levaditi's method show no spirochetes.

Microscopic examination of the lungs shows a subacute bronchopneumonia in both lower lobes. The mucosa of most terminal bronchi in these lobes is partially or completely ulcerated containing a polymorphonuclear exudate mixed

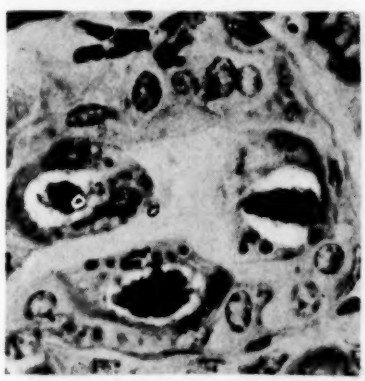

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Fig. 15.—Large cells in epithelial wall of serous salivary gland of guinea-pig. Note dark irregular intranuclear body, clear nuclear space and spherical bodies in cytoplasm. Such spherical cytoplasmic bodies were very prominent in case reported by Jesionek and Kiolemenoglou.

Fig. 16.—Large cell partially lining alveolar wall of lung. Opposite it are epithelial cells containing enlarged acidophilic intranuclear bodies.

Fig. 17.—Large cell free in convoluted tubule of kidney.

Fig. 18.—Group of three large cells between renal tubules.

with some fibrin and cellular debris. The bronchial walls are thickened by edema, an exudate of mononuclear cells and by fibroblasts. The smaller veins and capillaries are dilated. Neighboring alveoli are often compressed or filled with cellular exudate in which a few streptococci are present. There is an irregular consolidation of intervening alveoli by purulent exudate, a little fibrin

and desquamated epithelial cells. Irregularly distributed throughout the inflamed lung are a great many large cells conforming in appearance to the descriptions of the protozoan-like cells given by the above mentioned observers. These cells are present most numerously within the walls of chronically inflamed bronchi, but are to be seen also in considerable numbers within the epithelial lining and free in the lumina of alveoli. They are usually round or oval in shape, but may be elongated and irregular in outline, depending on their situation. Those within alveoli are more likely to be round or oval, while those in bronchial walls may be quite irregular. They measure from 10 to 30 microns in diameter. No distinct cellular capsule, as described by Jesionek and Kiolemenoglou is to be seen. Each cell contains a very large nucleus separated from the cytoplasm by a sharp membrane. In the center of the nuclear area is a large acidophilic body which sometimes appears dense and homogeneous, sometimes delicately honey-combed. It may have a central denser portion with a lighter periphery. There is a clear unstained space between the central nuclear body and the nuclear membrane in which usually are seen dark, dense, basophilic, often spherical granules, only two or three of which are to be seen, as a rule, in a single section through the cell. One may be situated at each pole of the central body, or they may be irregularly arranged about the nuclear membrane. The cytoplasm of these cells is variable in appearance. It is more basophilic than neighboring tissue cells, may be reticular or may contain rather large spherical basophilic granules or vacuoles. Usually eosin staining granules and thin rods can be seen within it in preparations stained by the eosin methylene blue method after fixation in Zenker's fluid.

COMMENT

One observing well developed cells of this type, can hardly recognize a resemblance to any normal cell of the body, but within the walls of the bronchi in these lungs it can be readily seen that they arise from a metamorphosis of certain tissue cells which lie just outside the endothelial lining of small veins and capillaries. These perivascular cells belong to the group of so-called "large mononuclear wandering cell," and are probably derived in this case from endothelium. They possess an oval or slightly horse-shoe shaped vesicular nucleus and a reticular lightly basophilic nongranular cytoplasm. The first evidences of change in them is the appearance of a small eosin-staining intranuclear body having characteristics of a nucleolus. The nuclear chromatin aggregates and the nuclear mass seems clear and empty. Coincidently the cell increases in size and the cytoplasm takes a more deeply basic stain. Sometimes eosin-staining granules or fine rods can be seen in the cytoplasm. The central nuclear body continues to enlarge, and with it the nucleus and cell body greatly increase in size until they become relatively huge. The nucleus may be horse-shoe shaped, containing an elongated, similarly shaped, intranuclear body. Cells at this stage of change appear sometimes partially to line a small vein or they may be entirely free within the vascular lumen, occasionally completely filling a capillary. Likewise they may occur between epithelial cells of a bronchus or within a bronchial lumen. They are usually single, but may be in groups of three or four, especially in alveoli.

Evidently after gaining entrance to the blood stream through the endothelium of bronchial veins they are carried in the blood current to the kidney where they can be found here and there lodged within glomerular capillaries. That they can in some way penetrate capillary walls is indicated by their occurrence also within convoluted renal tubules where they lie free within the lumen. Occasionally, one or two are found in the interstitial tissue outside a tubule which contains similar cells. There is no inflammatory reaction about them in the kidney. An occasional cell of this type is seen in the liver in a portal area, probably having been borne there through the blood stream and lodged within a capillary. No inflammatory reaction is present in the liver. No cell of this type has been observed in organs other than lung, kidney and liver.

The origin of the cellular change in the lung seems to be directly related to the chronic inflammatory process in bronchial walls. In areas of more acute inflammation such cells are not found. In most of the cases previously reported there was also an associated chronic lesion, three instances of possible congenital syphilis and one of pneumonia quite similar to that described here. The cause and significance of this singular metamorphosis is not clear, but it is apparently a retrogressive manifestation, for many such cells can be seen to be disintegrating, and there is no evidence whatever that multiplication can take place. The great size of the cells at first suggested the possibility of their origin from megakaryocytes, but in capillaries within areas of more acute pneumonia normal bone marrow giant cells were found; and the cells under consideration have no likeness or relation to them.

While it is clearly evident that certain perivascular tissue cells in the bronchial walls become transformed into the so-called "protozoan-like" structures, it is not certain that all of them are derived from this source. The possibility of other types of cell, particularly epithelium, undergoing a similar transformation should not be ignored. Occasionally, one can see changes in nuclei of alveolar epithelium in the above described lung which suggest that they too may be undergoing the same alteration of character. Certain of these epithelial cells contain large eosinophilic intranuclear bodies surrounded by a clear zone, but no undoubted examples of transition have been observed. The two instances recorded by Ribbert in which the large cells were present within ducts of the parotid gland without evidences of inflammation also suggest the possibility of such an epithelial transformation. Recently Jackson [4] called attention to certain structures occurring within epithelium lining ducts of salivary glands of guinea-pigs, which we have little hesitation in saying are examples of a cellular transformation

4. Jackson, L.: J. Infect. Dis. **26**:347, 1920.

similar to that occurring in the above described lesions of infancy, although they were regarded by her as protozoan parasites. We have studied a number of our own preparations of salivary glands from apparently normal guinea-pigs which contain these bo s, and while there are minor differences of structure, the change appears to be essentially the same as in the lesions of infancy. We have observed them only within ducts of serous glands, and there may or may not be an attendant focus of mononuclear cells near. There is no evidence of transition of epithelium lining the ducts, but when these cells are regarded as altered tissue cells and not protozoan parasites, the possibility of their origin from epithelium becomes obvious.

It is difficult to formulate an opinion as to the nature of this remarkable cellular change. The earliest recognizable alteration in the transition forms is the prominence of the acidophilic intranuclear body which in well developed stages becomes perhaps the most conspicuous structural component. A somewhat similar structural variation in the intranuclear body has been described by Tyzzer [5] in cutaneous lesions of varicella. In the region of epithelial vesicles the intranuclear bodies of different varieties of cell, including epithelium and endothelium, becomes very prominent and resembles in certain respects those found in early stages of the protozoan-like cells. Certain cells thus affected may enlarge and through amitotic division become multinucleated. Influenced largely by the structural prominence of the intranuclear body in the large cells of the infant's lung, one is tempted to suggest that the nucleolus may be the site of the initial change and under its diseased influence the cell as a whole may change in structural properties.

In the above described lesions of the lung the large cells appear to be secondary to the subacute pulmonary inflammation and apparently are a result of it. There is a possibility also that in the other recorded cases their occurrence was secondary to inflammatory changes of one sort or another. That their appearance in any way influenced the intercurrent disease does not seem at all probable. The arrested development and fibrosis of the pancreas, the glycosuria and renal functional disturbances do not seem to be in any way directly connected with the cellular anomaly.

Demonstration of the origin of these unusual structures from tissue cells adds to pathology a new kind of abnormal cytomorphosis, manifested by morphologic peculiarities entirely unknown in adult human lesions. Cellular gigantism is familiar in certain tumors, but not even the many morphologic vagaries of cancer have simulated the structure of these abnormal cells of infancy.

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5. Tyzzer, E. E.: The Histology of the Skin Lesions in Varicella, Philippine J. Sc. **1**:4, 1906.

While the conspicuous character of these cells may cause them to dominate the microscopic picture, their presence hardly indicates a disease entity, but rather they seem to represent an effect of chronic inflammation upon certain cells which may not be so stable in infancy as in adult life. The possibility of an unknown intracellular infection stimulating the cells to assume this unusual structural variation has at present no evidence to support it.

This cellular change is of such a characteristic nature that there is no difficulty in recognizing it when present, but as heretofore it has not been recognized as a metamorphosis of tissue cells, it seems advisable to identify the condition with a descriptive name, and we would suggest that it be called *cytomegalia* to emphasize the notable enlargement of the cells affected, and at the same time to distinguish it from those forms of cellular enlargement which at present are included under the general term giant cells.

REPORT ON A CASE OF GAUCHER'S SPLENOMEGALY *

N. CHANDLER FOOT, M.D., AND WILLIAM E. LADD, M.D.

BOSTON

Up to the present time only twenty-one cases of this unusual disease have found their way into the medical literature. First described by Gaucher,[1] in 1882, it was not mentioned again until 1895, when Picou [2] published his first article, followed by a second,[3] in conjunction with Ramond, in 1896. Collier,[4] in England, had, in the meantime, published a report in 1895. Bovaird [5] was the first to describe it in America, and it was only in 1906 that Schlagenhaufer [6] reported the first German cases. F. S. Mandelbaum, of New York, has undoubtedly done the most to put the pathologic peculiarities of the disease on a sound footing.[7] Working alone and with various collaborators, notably Brill (who published two articles independently [8]) and Downey, he has given a most comprehensive survey of the clinical and pathologic aspects of these cases.

According to him, the disease occurs oftenest in childhood, may be familial, is accompanied by progressive enlargement of the spleen (which may attain colossal proportions) and is followed by a similar enlargement of the liver. There are frequently brownish-yellow discolorations of the face, neck and hands, wedge-shaped thickenings of the conjunctiva, like pinguecula, usually beginning on the nasal side and appearing later on the temporal, their apices at the outer rim of the cornea. The disease has a prolonged, chronic course, with surprisingly little disturbance of function. Later, there may be a tendency toward

* Received for publication, Dec. 7, 1920.

* From the Children's Hospital and the Department of Comparative Pathology, George Fabyan Foundation.

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bleeding from the nose, bowel or uterus; leukopenia, and, ultimately, anemia of the chlorotic type. Occasional symptoms are persistent sweating and abdominal pain or pain in the legs. Females have been more affected than males, although more male cases have been reported recently, which has somewhat altered the ratio.

The disease is very insidious in its onset, slight dragging pain or enlargement of the spleen may be the first symptoms noted. The average blood count shows: Hemoglobin 65 per cent., (from 35 to 92 per cent.); erythrocytes, 6,000,000, later 3,700,000; leukocytes slightly decreased. Differential count: Polymorphonuclears, 66 per

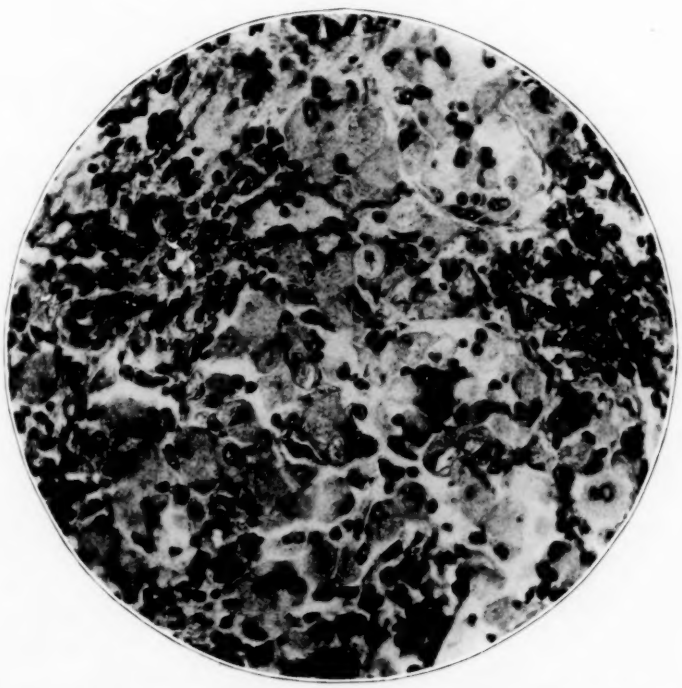

Fig. 1.—Paraffin section, phosphotungstic acid-hematoxylin, × 400. Gaucher cells in their usual alveolar arrangement. Note vacuoles and striae in several.

cent.; macrolymphocytes, 13 per cent.; microlymphocytes, 20 per cent.; eosinophils, 1 per cent.; mast cells, from 0.5 to 0.8 per cent. The large cells peculiar to the disease are never found in the circulating blood; there are no nucleated red cells. The duration is 19.3 years on the average, it may be much longer, the patient usually dying from some intercurrent infection.

Pathologically speaking, the disease is limited to the hematopoietic system; beginning in the spleen, it spreads to the regional lymph nodes of the mesentery and retroperitoneal groups, involves the bone marrow

and appears in the radicles of the portal vein and in the perilobular connective tissue of the liver, where it is, therefore, confined to Glisson's capsule. The spleen is usually much enlarged, it may extend from the diaphragm to the left iliac fossa. It is usually smooth, firm and apt to show one or more deep notches in its anterior margin. On section, the color is generally pale, grayish pink with minute, semitranslucent areas about 1 mm. in diameter scattered uniformly over the cut surface. Often there are hemorrhagic areas of small size. Rarely, there is evidence of necrosis, but only where tuberculosis

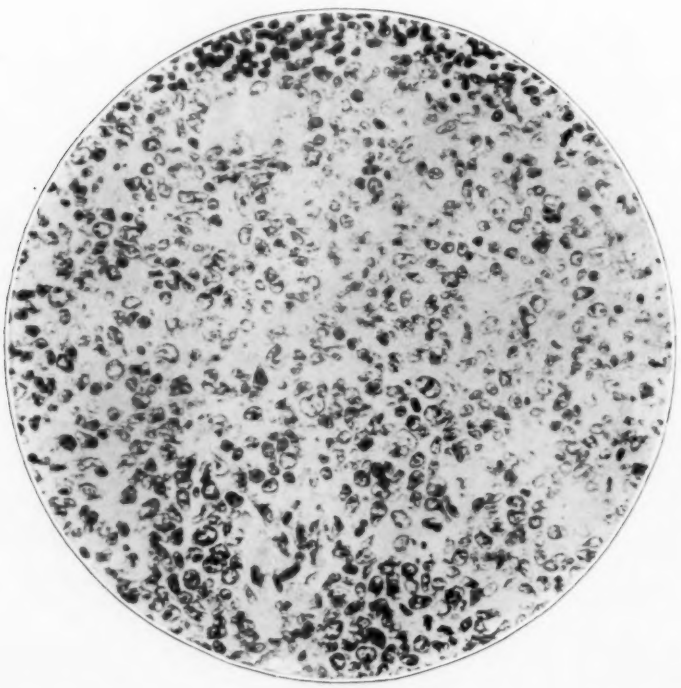

Fig. 2.—Paraffin section, phosphotungstic acid-hematoxylin, × 400. A "germinal center" from the spleen, showing several mitotic figures, and near 2 o'clock, three "tingible Körperchen" in a cell.

was associated with the lesions (Schlagenhaufer, loc. cit.). The liver is enlarged, and on section shows a fine network of pale, slender strands running between the lobules and outlining them in grayish-white. It is brownish in general tone and cuts with increased resistance. The lymphnodes of the mesentery and retroperitoneal region are enlarged and pale, and, on section, show a picture somewhat similar to the cut spleen. The bone marrow is grayish-red and thickly strewn with tiny, whitish specks, similar to those seen in the spleen and lymphnodes.

The microscopic picture is similar in all these organs; there are a great many large ovoid cells with small nuclei and somewhat vacuolated cytoplasm, usually lying in venous or lymphatic sinuses, or in the meshes of the tissue in question. They will be described at length later on, in the cases of the spleen; they are discussed in great detail in connection with the other organs involved, in any of the longer articles referred to in the list of references given in this paper.

Our case occurred in a boy, aged 8 years, who was admitted to the Children's Hospital suffering from persistent sweating, sudden loss in weight and anorexia. A mass was made out in his left hypo-

Fig. 3.—Frozen section, Bielschowsky-Maresch impregnation, × 400. Showing the delicate reticulum of fibrillae and the anastomosing Gaucher cells through which they run.

chondrium, but no definite diagnosis was arrived at until an accessory splenule, removed during an explanatory laparotomy, was diagnosed as typical of Gaucher's splenomegaly. It will be noted from the history that most of the typical symptoms were absent, while several of those usually considered occasional were present. These facts, together with the vague history of gastro-enteric disturbances and epileptoid seizures, made the clinical diagnosis of the case extremely difficult.

REPORT OF CASE

History.—The patient, Albert B., 8 years of age, was admitted to the surgical service in May, 1920. His anamnesis is compiled from data given by the parents at this time and from notes made by various observers in the Outpatient Department, where he had been an occasional visitor since 1915.

Family History.—His family history is negative; his parents and five brothers are alive and well, no deaths, no tuberculosis, cancer, insanity, nor hemophilia.

Previous History.—Birth normal, breast-fed. Between the second and fifth years of his life he had five attacks of unexplained unconsciousness, diagnosed by the neurologists as "probable epilepsy." He was first brought to the Outpatient Department in January, 1915, and again in June of that year. Both times the complaint was loss of weight, anorexia and restlessness—particularly

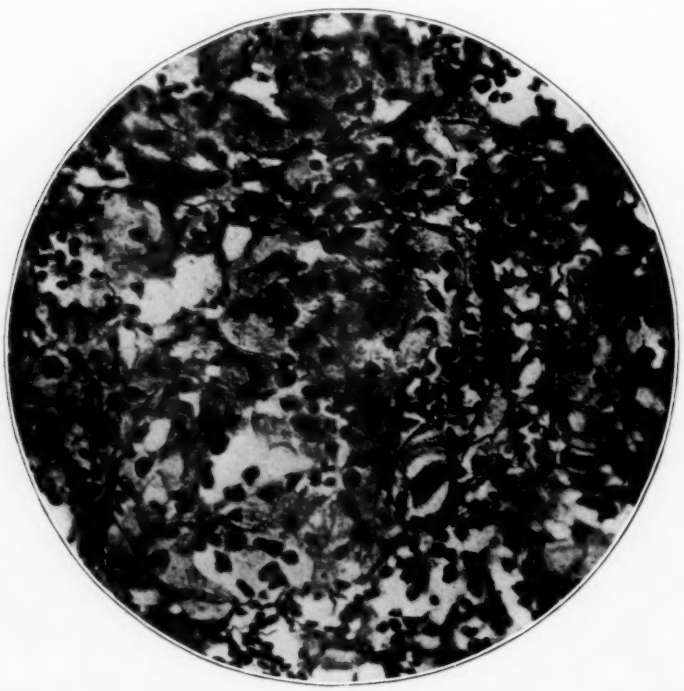

Fig. 4.—Thicker frozen section, Bielschowsky-Maresch impregnation, ×400. Showing alveoli and also the anastomosing type of arrangement of the Gaucher cells. Note the coarse, undulating fibrils of the more normal pulp reticulum and the straighter, finer fibrillae of the Gaucher cell cytoplasm.

at night. Diarrhea was the outstanding symptom at the second visit. In July, 1916, he had lost 3 pounds in weight and was suffering from "feverishness" and severe headaches. He had had two of his unconscious spells since the preceding visit and had had chickenpox. A fulness of his left flank was noted on physical examination at this time.

He was not heard from again until September, 1918, when he came back with a history of persistent vomiting and poor appetite. In May, 1919, he was suffering from profuse sweating, both at night while in bed, or in the daytime after the slightest exertion. He had severe frontal headaches daily, most severe

in hot weather, was nauseated, but did not vomit until the day before he was brought in. He had night terrors and was very irritable. On physical examination his spleen was palpable 1 cm. below the costal margin, in the nipple line.

In June, 1919, he was re-admitted, suffering from traumatic synovitis of the knee, which was noticeably stubborn. At that time his spleen was noted as being "just palpable." In September, 1919, an irregular, doughy mass, feeling more like impacted feces than a spleen, was palpable in his left hypochondrium. This was apparently unconnected with the spleen, as it could be rolled under the fingers, was freely movable and did not move with respiration. His liver was just palpable below the right costal margin. A blood count, made at this time, showed, hemoglobin, 80 per cent.; leukocytes, 9 600. Differential Count: normal.

Present Illness.—In April, 1920, he was examined at the Outpatients' Department and sent to the hospital. He had been feeling moderately well, but had just recovered from mumps and measles. His appetite was now very poor, he had pain in his entire body after playing, most marked in the abdomen, occasional morning vomiting and perspired excessively. When put to bed he would be restless and perspiring and would not go to sleep until late, sleeping late in the morning. He was not attending school on account of his extreme nervousness and his vomiting. He complained of seeing "colored balls" before his eyes and "having shocks" over his entire body. On admission to the hospital the chief complaints were sudden loss of weight and excessive perspiration.

Physical Examination.—On admission this was negative, save for a large, smooth, painless, movable tumor in the left hypochondrium. The dulness extended upward to the angle of the left scapula and 8 cm. to the left of the midsternal line. The tumor was palpable 4 cm. below the costal margin in the left nipple line. The left flank was fuller than the right. Shortly after admission the house surgeon noted: "Large tumor in left side; opinions differ as to whether this is spleen, kidney, or some neoplasm."

His blood count at this time showed: Hemoglobin, 90 per cent.; erythrocytes, 5,808,000; leukocytes, 6,600: Differential Count: Polymorphonuclears, 49 per cent.; macrolymphocytes, 19 per cent.; microlymphocytes, 30 per cent.; mononuclears, 3 per cent. One myelocytic neutrophil was noted. His von Pirquet test was positive but indefinite to bovine, negative to human tubercle bacilli. Wassermann was negative. His temperature was subfebrile, averaging from 99 to 100 F.

Treatment.—An exploratory laparotomy was performed May 10, 1920, revealing a large, smooth spleen and two accessory splenules, one of which was excised from the omentum and sent to the pathological laboratory. The report was "typical of Gaucher's splenomegaly." Accordingly, June 1, 1920, the spleen and the remaining splenule were removed. The patient made an uneventful recovery; the stitches were removed on the eleventh day and he was discharged the day following. He was seen Oct. 15, 1920, and found to have gained 8 pounds and to be much improved in health. His sweating had practically disappeared, his digestive disturbances were not marked, and he could attend school regularly. Just before his discharge from the hospital his blood count showed: Hemoglobin, 80 per cent.; erythrocytes, 4,976,000; leukocytes, 18,800. Differential Count: Polymorphonuclears, 48 per cent.; lymphocytes, 41 per cent.; mononuclears, 10 per cent., and eosinophils, 1 per cent. No abnormal red cells were present.

Pathologic Reports.—May 10, 1920. A small nodule, bright red in color, enclosed in a small mass of omental fat, resembled an accessory spleen; is lens shaped; measures 0.6 cm. in diameter and 0.4 cm. at its thickest portion.

Microscopic Examination: Rudimentary splenic tissue, with poorly defined trabeculae and splenic corpuscles. There are no nodules or marginal sinus, like those of a lymph node. The sinuses and pulp spaces of this little spleen are filled with large, vacuolated or reticulated cells, which contain occasional inclusions.

Operation.—The large spleen proper and the remaining accessory spleen were removed, June 1, 1920. The spleen weighed 305 gm. and measured 14 by 6 by 5 cm. It was markedly lobulated, with two distinct notches and a smooth capsule. Outwardly of an almost normal color (reddish-purple), it was pale, pinkish-buff on section. The cut surface was marked with small, semitranslucent masses about 1 mm. in diameter, and the splenic corpuscles stood out reddish on a pale background, the reverse of normal. The consistence was firm and rather waxy; the pulp did not strip on the knife edge. A smaller, accessory spleen accompanied the specimen. It was about the size of a small filbert, 1.5 by 1 cm. Its appearance, consistence and color, correspond to those of the larger organ.

Microscopic Examination of Spleen.—The microscopic architecture of the spleen was so strikingly altered by the interpolation of the large cells typical of this condition, that one would scarcely recognize it at first glance (Fig. 1). There were countless numbers of these cells everywhere, filling the venous sinuses and pulp spaces so completely as to transform the picture into one resembling an alveolar tumor. They vary from 17 to 35 microns in diameter and are roughly ovoid in shape; their cytoplasm is usually pale, but here and there one finds cells with a more homogeneous, deeply staining protoplasm. As a rule, however, they show a pale, reticulated structure with the fibrils running in a longitudinal and roughly parallel fashion, from pole to pole of the cell. They often contain inclusions of a hyalin nature, which will be described presently. The nuclei resemble those of the reticular cells, or of the endothelial cells, in that they are vesicular, show a delicate chromatin reticulum and one to three larger masses of basophil material, like nucleoli. In the eosin methylene blue sections prepared from this spleen, there is a tendency toward eosinophilia on the part of these nuclei, as is also the case with those of some of the reticular cells. The endothelial nuclei, in cells lining sinuses, do not show this, but stain deep blue.

Mitotic figures are extremely rare in the Gaucher cells; only one was found after prolonged searching. These cells fill both the venous sinuses and the pulp spaces so full that it is extremely difficult to tell the former from the latter. There are no such dilated sinuses with a comparatively clear lumen, filled mostly with erythrocytes, as pictured in most of the cases in the literature. The whole field, in our case, seems to be composed of irregular alveoli filled with large, pale reticulated cells. The inclusions just spoken of are in the form of hyalin masses or droplets in the cytoplasm of the Gaucher cells. They give practically the same staining reaction as does collagen: bright red with eosin methylene blue, brownish red with Van Gieson's stain and phosphotungstic acid hematoxylin sections, indigo blue with Mallory's anilin blue connective tissue stain, dirty to bluish green with Weigert's elastic tissue stain and blue with ferrocyanid of potash. In unstained section they are rather faint brownish yellow. They do not react with sudan III nor Nile blue. They are not confined to the cells, but lie about among them and apparently fill the cytoplasm of the smaller cells of the familiar endothelial phagocytic type, the nucleus being crowded to one side. Or, sometimes, no nucleus can be made out and the bodies appear like empty hulls; for this reason they seem, at first, to be artefacts, but after more careful study this does not appear to be so. They seem to exist, at first, as small branching masses of what looks, at first glance, to be fibrin; these gradually appear more swollen and hyalin and are taken up by the cells. The hull-like structures are probably the "shadows" of these cells after they have become necrotic; one often finds them badly wrinkled, or shriveled, their nuclei obviously in the last stages of karyolysis.

One occasionally finds erythrocytes which have apparently been phagocytosed by the Gaucher cells, lying in vacuoles in the cytoplasm of the latter; so many lie on, rather than in the cells, that this must be stated with reservations. There are also two forms of pigment in the cytoplasm of the Gaucher cells; a

very faintly yellow granular form and an apparently diffuse and almost invisible one, both of them containing iron in a free state. They scarcely would have been noticed in this case, if one had not read of them elsewhere and tested for them chemically. Two familiar lipoid stains were used to determine the presence of fat or lipoids in the Gaucher cells, but without success. Sudan III demonstrated no granules, and Nile blue, while staining some of the cells more deeply than others, gave no typically granular reaction. In the face of this evidence, there is no need for employing other and more complicated lipoid stains.

Having disposed of the description of these cells, little is left to say about the lesion; the splenic capsule and trabeculae are not much thickened, the amount of elastic fibers is apparently normal, there is no increase in connective tissue elsewhere in the organ. The malpighian corpuscles are, as a rule, small; they are not much altered, here and there one finds one with a larger, well developed germinal center (Fig. 2) which shows active mitosis among the macrolymphocytes. Occasionally, these cells are larger and more vesicular than usual and rarely one finds gigantic cells of this type with very large, somewhat lobulated, vesicular nuclei, as described by Mandelbaum and others. Gaucher cells, or cells similar to them, are found lying singly near the periphery of the centers and containing many small, basophile bodies (Flemming's "tingible körperchen," Mandelbaum[7]). Occasionally, the lymphoid reticulum is swollen and hypertrophic. In this case there are comparatively few Gaucher cells in the germinal centers.

There is a network of strands of more normal pulp between the alveoli of Gaucher cells. Here one finds a marked increase in eosinophil leukocytes, of both polymorphonuclear and myelocytic types. Plasma cells are abundant. Occasionally one finds typical megakaryocytes and cells somewhat resembling them, but more like the "Dorothy Reed" or "Sternberg" type of tumor giant cells of Hodgkin's granuloma. The endothelium of the venous sinuses tends to desquamate abundantly and to become very hydropic and swollen. There are many cells resembling plasma cells, only much larger and apt to have irregular, ameboid outlines. Their nuclei are of the lymphocytoid type, their cytoplasm dense and slightly basophilic. One cannot fit them into a transition-scale between lymphocytes and the Gaucher cells. This sums up the pathology of the spleen, that of the two accessory spleens is quite analogous.

DISCUSSION

Since Bovaird described his cases, no one has attempted to put the Gaucher cells into any category other than that of the endothelial cells; opinions have differed as to whether they are purely endothelial, or whether descended from the reticulo-endothelial cells. The trend has been steadily toward the latter derivation and, in our case at least, this seems justified. It has already been stated that their nuclei and those of the reticulum tended to slight acidophilia in the eosin methylene blue preparations and that the reticulum of the germinal centers seems swollen and hypertrophic. This is also true of the adventitial cells of the smaller arteries.

Fortunately, a portion of the spleen frozen and cut for the Bielschowsky-Maresch silver impregnation showed a somewhat earlier stage in the disease than did the others (Fig. 3). Here the large cells are arranged in columns, or branching rows and in some places they are found to be stellate and to anastomose with one another. In these sections there is more normal pulp present, and the malpighian

corpuscles show very little deviation from the usual form. Thin sections from these blocks show a delicate network of reticulum fibrils with the Bielschowsky-Maresch method (Figs. 3 and 4). These fibrils run through the cells and not over them, when found in the stellate, anastomosing type. In the alveoli they surround the Gaucher cells very intimately (Fig. 4). Risel [9] stated that the large cells could be disengaged from this network readily, by slight pressure on the coverslip. It was found, in our preparations, that very rough treatment, such as grinding the section between the coverglass and the slide with one's thumb and forefinger, was necessary to break up the tissue and, even then, many of the Gaucher cells remained sticking together in groups of three or more. Some of them did, indeed, come out clear and discrete; but many still showed coarse fibrils in their cytoplasm, or adhering to their periphery. Shaking up such sections with glass beads in glycerin, for an hour, failed to break out any but an insignificant number of these cells, although many leukocytes and lymphocytes were liberated. There is no doubt that the majority of these cells are firmly bound together by a fine reticulum. Whether they produce it or not is, at best, a matter for speculation and deduction, rather than an observed fact. The odds are, however, strongly in favor of reticular origin.

This case, then, fulfills the requirements as postulated by Mandelbaum and Brill.[7] The large cells contain no lipoids, they do contain iron compounds showing the typical reaction to potassium ferrocyanid; both diffuse and granular. The various inclusions described are all present here, except that no iron-free pigment is demonstrable. Reticulum fibrils are found in the younger, anastomosing Gaucher cells and the columnar arrangement described by Mandelbaum (in connection with lymphnodes) is found here in the spleen.

It is interesting to note that the clinical symptoms in our case are rare ones, rather than the more usual variety. There was no cutaneous discoloration, no tendency to bleed, little enlargement of the liver and no conjunctival symptoms. Enlarged spleen, pain in the abdomen and legs and profuse sweating were present. The blood counts were not particularly significant, and there was a long history of gastro-intestinal disturbances which might be referable to lesions in the lymphoid apparatus of that tract, but which must remain, for the present, problematical. There seems to be no other case in the family. The child's spleen was first enlarged and palpable when he was 7 years old, the disease making, therefore, greater strides in the last twelve months than in the preceding three years elapsing since a "full-

9. Risel, W.: Beitr. z. allg. Path. u. z. path. Anat. **46**:241, 1909.

ness in the left flank" was noted. The immediate results of the splenectomy have been most encouraging; it remains to be seen how the case will conduct itself as time goes on.

In a disease of such rarity and which runs so long a course, the advisability of radical operation must, necessarily, be still debatable. But if the theory is correct that the disease originates in the spleen and then spreads to the lymph nodes, liver and bone marrow, it is logical to bend our efforts toward making an early diagnosis and resorting to splenectomy as soon as possible. If, on the other hand, the enlargement of the spleen is a manifestation of some metabolic change of which we are at the present time ignorant and which will continue, in spite of the removal of the spleen, to affect the liver, lymphnodes and bone marrow, it is obvious that we can not expect a permanent cure from splenectomy. However, we know at the present time that the disease is fatal if untreated, or if treated by any means other than radical operation; we likewise know that splenectomy will afford very marked temporary relief from symptoms and improvement in general health. With these facts in view early splenectomy is, therefore, the treatment to be for the present recommended.

The literature [10] on this subject is, as a whole, well written, and almost any of the more recent articles will give the reader a good description of the disease; those of a Mandelbaum, Schlagenhaufer and Risel are the most complete. Several cases have been reported as Gaucher's splenomegaly which were, in reality, of a different type and due to lipoidemia. Among these are those of Knox, Wahl and Schmeisser and De Lange and Schippers; the reasons for excluding them, as well as the exact references, will be found in Mandelbaum and Downey's article.[7]

When one comes to a consideration of what causes the disease, there is very little to say. We do not even know what processes it represents. Gaucher thought it an epithelioma. In the nineties it was considered an endothelioma. Bovaird was the first to advance the theory of its being due to some toxin of unknown origin, and Mandelbaum, in his last article says: "The disease is evidently caused by some disturbance of metabolism, the products may be of a combined protein-lipoid nature, not to be grouped among 'extractives' and for which no microchemical test has yet been devised." One might be tempted to consider the process as a tumor of the reticular tissue, starting in the spleen, spreading to the hematopoietic system in the lymph nodes and bone marrow and metastasizing to the perilobular hepatic connective tissue of Glisson's capsule. But there is too much evidence on the other side of the argument and too many points against neoplasia to permit one's siding with the earlier writers on this subject. The spleen

and lymph nodes are not involved locally, but the whole organ undergoes this change. The cells show no true metaplasia, there are extremely few mitotic figures and the normal structure of the organs affected is always in the background; there is no true replacement by new tissue. We must, therefore, fall back on Mandelbaum's hypothesis as the most tenable; it is unfortunate that the condition is so rare that more cases cannot be studied in a systematic fashion, particularly from the chemical standpoint.[10]

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10. In addition to the references already given, the following are also of interest:

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Erdman, J. F., and Moorhead, J. J.: Am. J. M. Sc. **147**:213, 1914.

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Marchand, F.: München. med. Wchnschr. **54**:1102, 1907.

Reuben, M. S.: Am. J. Dis. Child. **5**:28 (Jan.) 1912; ibid. **8**:336, 1914; ibid. New York M. J. **107**:118, 1918.

A CASE OF IDIOPATHIC HEMORRHAGIC SARCOMA OF KAPOSI *

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NEW YORK

In 1872, Kaposi brought to notice an unusual and remarkable affection of the skin which was characterized by the occurrence of deeply pigmented infiltrated areas and small tumors situated generally in the extremities and often followed after several years by visceral metastases and death. Since then, many reports of cases have been published similar in certain aspects to Kaposi's type but characterized, on the whole, by wide variations from the original examples. In a search through the literature few cases in children have been discovered, and none of these are described in sufficient detail to invite comparison with the case herein reported.

The child was examined by a number of physicians, none of whom had seen a comparable condition in either a child or an adult. A variety of opinions were advanced regarding the probable diagnosis, but it was finally decided that it more nearly resembled the type described by Kaposi than any other.

REPORT OF CASE

R. B., 5½ years old, of Jewish parentage. Both mother and father were healthy and were born in the United States. The child was referred from the office of Dr. L. Emmett Holt Feb. 20, 1920, for admision to the Babies' Hospital and was under observation on his service for twenty-four days.

The patient was the third of three children; the others were apparently normal in every respect. Prior to the onset of the present illness the child had been healthy, well nourished and well developed. Seven weeks before admission to the hospital the child could walk freely, but had gradually become so weak that when seen in Dr. Holt's office he was only able to walk a few steps.

Previous History.—The father states that about seven months previously, a purple spot about the size of a thumb nail appeared on the left cheek. This grew very slowly, and at the end of three months it was about the size of a silver quarter, the color remaining the same. Shortly afterward the whole right cheek gradually became swollen and discolored. About six weeks after the spot was first noted on the left cheek, the father noted the appearance of other spots on the buttocks, hands, arms, legs, feet and body. He had observed that these spots had been appearing and disappearing to date. It has been further stated by the family that the swelling of the face had persisted since first observed but that at times it had been more marked than it was at the time of admission to the hospital. A few weeks after the onset of the disease epistaxis occurred and on another occasion there was a slight hemorrhage from the bowels.

The child had been treated at another hospital three months previously and while there received three transfusions. After the second transfusion the temperature rose to 106 F. and was accompanied by considerable swelling of the face.

* Received for publication Jan. 12, 1921.

Physical Examination.—On examination the child was found to be moderately well nourished and well developed. The mucous membranes seemed markedly anemic. Both cheeks were greatly swollen and hard and tense to the touch. There was a symmetrical deep purplish discoloration of the face not limited to the swollen cheeks but extending above to the lower lids and below to the lower lip and chin (Fig. 1.) On the left side of the face there was a marked induration extending from the cheek. It involved the cellular tissue of the whole of the left side of the face, extending as high as the external auditory meatus. This brawny area was also discolored, but the pigmentation was less intense than over the cheeks. A similar condition existed on the right side, but it was limited almost entirely to the right cheek with an isolated

Figure 1

patch in the middle of the supraorbital ridge. The lips were indurated and pigmented, particularly the lower, the induration was so marked that the child constantly kept the mouth partially open. The chin was discolored and indurated, but not to the same degree as the cheeks. There was a slight hemorrhage in the subconjunctiva of the left eye.

There were a number of subcutaneous masses, not sharply outlined, over the frontal region, and a few spots on the scalp about the size of a pea, all of which were purplish in color. The chest presented some faintly discolored

areas of a different character about the same size as those on the scalp, but these were not indurated. There were also a few spots on the upper chest and extensor surfaces of the arms and forearms which were apparently in the fading stage. Over the thighs and buttocks there were some spots similar in character to those on the chest and arms, one of which was indurated. The tonsils were hypertrophied, and a few hemorrhagic foci were noted on the tonsils and peritonsillar tissue.

All of the superficial lymph glands were slightly enlarged, but not tender on pressure.

Figure 2

A marked systolic murmur limited to the cardiac region was heard. It was evidently a hemic murmur. The apex beat was one-half inch inside the nipple line, the pulse rate was 136 and of fairly good quality. The abdomen was tympanitic with the distention mainly in the epigastrium. The lower border of the liver was felt about one inch below the costal margin and the lower pole of the spleen was one and one-half inches below the free border of the ribs.

Laboratory Examination.—The urine was found normal on several examinations, the Wassermann test was negative, the von Pirquet was negative and the guaiac test for occult blood in stools was negative on a number of occasions. The blood culture was sterile. The blood picture showed 25 per cent, hemoglobin, 1,288,000 red blood cells, with marked variation in size and shape. One nucleated red blood cell was present and a few irritation forms. The white blood cells numbered 2,400, and the differential count showed: polymorphonuclears, 21 per cent.; small lymphocytes, 52 per cent; large lymphocytes, 24 per cent., and eosinophils, 3 per cent. A number of blood examinations were made, each showing a progressive decrease in the total number of red cells, the count falling to 552,000 the day before death. The white count was not higher than 13,000 at any time, and at the last examination it was only 2,000. The coagulation time of the blood was eight minutes. The child was transfused with 180 c c of blood two weeks after admission, but no improvement was noted, beyond a transitory increase in the number of red blood cells.

Dr. E. S. Thompson, who examined the eyes, found in both eyes pallor of the optic nerves and depressed retinal circulation; vessels, small and pale; profuse pigment stippling over both retina with the choroidal vessels showing here and there. A low grade of retinal atrophy was present.

Clinical Course.—The child was under observation for twenty-four days after admission to the hospital, and during this entire period a distressing croupy cough was almost constantly present, which occasioned the child great discomfort. The cough was at times brassy in character, simulating somewhat the cough in adults caused by a large aortic aneurism. It was not influenced by posture. It was thought that the cough was caused by enlarged mediastinal glands.

During the period of observation, with the exception of the last few days, the child seemed moderately comfortable, except for the cough, with occasional attack of dyspnea and, at times, pain in the left side of the face.

The swelling of both cheeks became progressively more marked. The discolored areas on the face increased in extent, involving the ears and the forehead, particularly the left side (Fig. 2). Here were large irregularly shaped purplish areas with a considerable tendency to subcutaneous infiltration. Numerous new areas, averaging the size of a pea, appeared on the chest and extremities and a patch the size of a nickel was noted on the scrotum. These small patches on the body did not resemble the areas described on the face, their appearance simulated the fading stage of the eruption frequently seen in cerebrospinal fever. About two weeks after admission the left pupil dilated and remained so until the child's death.

The most striking change in the child was the rapid increase in the size of the cheeks (Fig. 2). The normal contour of the face was almost obliterated by the two symmetrical tumor masses. These masses projected beyond the tip of the nose. After a fortnight's stay in the hospital, the upper border of the masses showed small areas of softening; these softened areas did not increase in size.

Fresh subconjunctival hemorrhages occurred in both eyes (Fig. 2). Both upper eyelids became partially involved, and it was difficult, because of the increasing thickening of the upper lids, for the child to keep his eyes open. At the end of the third week, the child's condition began to grow suddenly worse, he had epistaxis, and vomited large amounts of bright red blood. It was noted about this time that many ulcerated areas in the mucous membrane of the mouth were present and that the uvula had almost entirely sloughed away. During most of the child's stay in the hospital, he had a constant but irregular temperature, generally about 102 F. A few days before death, the temperature rose to 103 F. and remained high until his death.

Death occurred twenty-four days after admission to the hospital, apparently from anemia with a terminal bronchopneumonia. Neither a necropsy nor removal of tissue sections was permitted.

DISCUSSION

Brayton [1] states that up to 1903, of seventy-five cases of this disease reported in the literature all but six were in males; since that time many cases have been reported, the majority of which were in Jews, generally males. No reported cases have been noted which resembled this case in all particulars, but almost all the conditions present in this case have been noted in a composite of other cases. In Cole and Crump's [2] case the lesions were symmetrical in distribution but began on the lower extremities instead of on the face. It is possible, that some earlier lesions on the lower extremities might have escaped notice in the case reported here. In Fordyce's [3] case epistaxis was present. He also noted that the epidermis was glossy in places as if from overdistention of the tumors. In his case there was a disposition for the tumor masses to undergo softening, apparently similar in character to the breaking down noted in this case.

All the cases described in Kaposi's [4] original monograph occurred in persons over 40 years of age and all died of the disease, although in some the condition ran a chronic course over a number of years. In the second case there was enlargement of the lymph glands, which was present in my case, but which has been mentioned by other authors as being seldom present. In Kaposi's case there was involvement of the lower lids and nose as well as of the extremities. He observed that "eventually the same sarcomatous masses occur in the mucous membrane of the trachea, the esophagus, the stomach and the intestines, particularly the large intestine." Epistaxis, brassy cough, hematemesis and bloody stools, which were present in my case, are strongly suggestive of the presence of visceral metastasis.

In Boyet's [5] case the lesions were present on all four extremities. In my case the lesions were also present on all four extremities but only during the few days prior to death was there any tendency for the lesions to spread to regions remote from the face. In many of the reported cases the lesions began on the lower extremities, gradually involved the upper extremities, then the trunk and finally the face, exactly the reverse of the course in this case.

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1. Brayton, A. W.: Idiopathic Multiple Pigmented Hemorrhagic Sarcoma Cutis of Kaposi: Report of New Case and Notes of Three Preceding Ones, Indiana M. J. **21**:480, 1902.

2. Cole, H. C. and Crump, E. S.: Report of Two Cases of Idiopathic Hemorrhagic Sarcoma (Kaposi): The First Complicated With Lymphatic Leukemia, Arch. Dermat. & Syph. **3**:38 (March) 1920.

3. Fordyce, J. A.: Multiple Pigmented Sarcoma of the Skin (Kaposi), J. Cutan. Dis. **9**:1, 1891.

4. Kaposi, M.: Idiopathisches multiples Pigmentsarkom der Haut. Arch. f. Dermat. u. Syph. **4**:265, 1872.

5. Boyet: Sarcomatose idiopathique de Kaposi, J. méd. de Brux. **10**: 270, 1905.

Bernhardt [6] comments on the fact that these cases are not all similar. In one of his cases, as in my case, there was involvement of the uvula and of the soft palate and some suggestion of involvement of the hard palate. He quotes Hollaender [7] who demonstrated a case before the Berlin Medical Society in which the hard palate, the tongue, the eyelids and the cheeks were the site of the lesions.

In Gilchrist and Ketron's [8] first case—the arms, face and ears gradually became involved, although the first lesion noted was on the outer side of the right leg. In their second case, as in my case, the lesion was first noted on the face. In their conclusion they state "our studies show that the lesions begin in the skin as angiomas, due to a proliferation of the interstitial connective tissue and endothelium which gradually obliterates the blood spaces, forming solid tumors. In the early stages these resemble, in some areas, young connective tissue, in other areas, sarcomata. From this beginning, then, as cutaneous angioma or later angiosarcoma, the disease spreads by metastases which first appear in the neighborhood of the primary lesion and later become widespread both in the skin and internal organs, leading, in many cases, to death."

The course of the disease as noted in my case follows closely this description, assuming, of course, that death was due, as indicated by the clinical course, to widespread metastases in the internal organs.

This disease has infrequently been noted in children. In Kolmer's case, reported by Fordyce, a girl, 8 years of age, several hundred tumors were scattered over the extremities and trunk, which underwent involution leaving behind pigmented scars. Involution of some of the tumors has been observed by a number of authors, and involution of all of the tumors in certain cases has been noted by many. In my case there was no tendency toward involution.

In other case reports the disease progressed more slowly as age advanced and seemed less severe in character.

Kaposi mentions the case of an 8 year old boy concerning whom Bilbroth had consulted him. In this child the disease began with a lesion on the leg, numerous other lesions developed, resulting in death.

Breakey [9] observed that young persons may succumb to the disease in the first or second year. He quotes Councilman, who called attention to the fact that the path of the metastases in this disease is almost always along the blood vessels.

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6. Bernhardt, R.: Sarcomata idiopathica multiplicia pigmentosa cutis (Kaposi), Arch. f. Dermat. u. Syph. **49**:207, 1890.

7. Hollaender: Berl. klin. Wchnschr. **35**:107, 1898.

8. Gilchrist, T. C. and Ketron, L. W.: Report of Two Cases of Idiopathic Hemorrhagic Sarcoma (Kaposi), J. Cutan. Dis. **34**:429 (June) 1916.

9. Breakey, W. F.: Multiple Pigmented Sarcoma Cutis; Oronycosis Fungoides, Which? Tr. Mich. Med. Soc. **19**:479, 1895.

A commentary on the wide range of symptoms manifested in these cases may be gathered from an observation of Brayton's regarding his case in which the tumor masses were sensitive to pressure and their growth was attended with pain. This symptom has rarely been noted by other writers. In my case pain was present at times in the left side of the face but the tumor masses were not sensitive to pressure.

INFLUENZAL MENINGITIS

WITH REPORT OF A CASE *

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The literature contains many observations on meningitis caused by an organism resembling the influenza bacillus. The relationship of this organism to the so-called true influenza bacillus of Pfeiffer is still a matter of controversy. We wish to report such a case of meningitis and describe the results of the study of the organism. A variety of interesting laboratory findings were made, but the picture of the purulent meningitis remained clear cut. The bacillus was isolated from the spinal fluid, blood, throat, nose and nasopharynx. Cultures were studied and animals inoculated. The spinal fluid yielded a four plus Wassermann and reduced colloidal gold suspensions in the syphilitic zone. Morphologically typical diphtheria bacilli were found in large numbers in a nasal culture. Death occurred ten days after the onset. A necropsy was not permitted.

REPORT OF CASE

History.—The patient was referred to one of us (I. A. A.) by Dr. Mary Shutan. The child was a white male, aged 17 months, whose symptoms became manifest three days before admission to the hospital. On the first day of the illness the temperature rose to 102.4 F., but the child played and seemed to be fairly well. The following day the temperature dropped after a warm bath, but the child was very restless and vomited after nearly every ingestion of solids or liquids. There was no vomiting the next day, but occasionally afterward. Besides crying and being restless, muscular twitchings were noticed the second day, but convulsions did not occur. The right drum membrane was found bulging, and paracentesis yielded thick pus. This was repeated on both ears before admission to the hospital, and each time pus was obtained. The temperature had been subnormal for more than a day before admission, but rose subsequently. The child became very cold; rigidity was present, and the mouth had to be forced open to insert food. Strabismus was first noticed on the third day. There was no urination for periods of twelve hours on two occasions.

The birth and feeding histories were not remarkable. The patient was the third child. The parents and two other children were apparently well, and there was no history of miscarriages. The child had scarlet fever four months previously.

Physical Examination.—The patient was well nourished. He was restless and appeared to be very ill. The veins of the face were somewhat dilated. The right drum membrane was red, and there was a purulent discharge in the canal. Cultures contained staphylococci but no influenza bacilli. The left drum

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* From the Sarah Morris Memorial Hospital.

was bulging and cloudy. There was an internal strabismus of the left eye; no ptosis or nystagmus. The pupils were equal and reacted to light. There was marked rigidity of the neck and extremities, and the spinal column was flexed with difficulty. The Brudzinski sign was positive, but the Kernig sign was negative. The reflexes were all very active, but no pathologic reflexes were noted. The chest and abdomen were not abnormal.

Laboratory Findings.—Blood examination on admission showed 5,120,000 red cells and 7,600 leukocytes, of which 72 per cent. were polymorphonuclears, 28 per cent. small mononuclears, 3 per cent. large mononuclears and 1 per cent. transitionals.

A morning specimen of urine was cloudy, specific gravity of 1.020; acid, and contained albumin but no sugar or acetone. There were many granular casts, a few leukocytes and occasional erythrocytes.

Throat cultures were twice reported free from diphtheria bacilli.

Spinal puncture on admission yielded 40 c.c. of turbid fluid under markedly increased pressure. A pellicle formed in five minutes. There were 3,500 cells

Direct smear of the spinal fluid sediment showing pleomorphism of the organism. The long thread form appears to be a series of influenza bacilli joined end to end by their cell membranes. Note the appearance of polar staining (methylene blue stain).

of which 84 per cent. were polymorphonuclears, 9 per cent. lymphocytes and 7 per cent. endothelial cells. The Noguchi, Ross-Jones and Nonne tests were markedly positive. The Wassermann test was reported ++++, and the colloidal gold test showed a reduction in the syphilitic zone.

Direct smears of the pellicle showed many polymorphonuclear cells and a gram-negative, bizarre, pleomorphic bacillus, some forms of which were long threads, others plump and tiny. Cultures yielded the same organism. Its further history is given below.

Subsequent Course.—The day following admission 15 c.c. spinal fluid was removed. This specimen was more turbid than the first, contained 10,000 cells and the same organism. At this time, ethyl hydrocuprein, 2 gr., dissolved in 8 c.c. of water was injected into the spinal canal.

On the third day since admission, the sixth of the illness, the temperature rose to 105.4 F. Despite this the child seemed bright, but was very restless. There was no Kernig sign, but the Brudzinski was slightly indicated. The

reflexes were markedly exaggerated, and the strabismus of the left eye was unchanged.

On the fifth day, the eighth of the illness, the temperature was 103.6 F. The child was comatose, and the Kernig and Brudzinski signs were now quite marked.

On the day before death, 10,000 units of diphtheria antitoxin was injected deep intramuscularly because of the finding of diphtheria bacilli in the nose the day before, despite the absence of clinical symptoms.

Attempts to obtain spinal fluid at this time failed although it was apparent that the needle was in the canal. It was concluded that the exudate had become too thick to escape through the needle inasmuch as postmortem examinations of influenzal meningitis reveal a thick, plastered exudate over the cord and brain.

In the course of the disease, at the hospital, the temperature varied between 103.8 and 105.8 F. The pulse varied from 135 to 170, and respirations from 32 to 60.

Bacteriologic Examination.—A blood culture made on the day preceding death contained influenza bacilli. Two dilutions were made in preparing the culture. One was contaminated with staphylococci. A positive result was obtained even in the dilution of 0.5 c.c. of blood to 20 c.c. of plain broth. The same pleomorphism was noted as in the spinal fluid. When subculture was made on chocolate agar, typical influenza bacilli were found, with an occasional long form.

Smears on blood agar yielded colonies of influenza bacilli from the nose, throat and posterior nasopharyngeal wall. A culture from the nose on Loeffler's medium yielded morphologically typical diphtheria bacilli.

A cultural study was made of the organism obtained from the spinal fluid. Direct smears contained slender, gram-negative bacilli of different lengths and widths. Culture on blood agar plates yielded fine, dew drop colonies with pleomorphic, gram-negative bacilli. No growth was obtained from the same fluid on plain agar or plain broth. Subcultures from the blood agar plate on chocolate agar yielded typical influenza bacilli, but a few thread forms were present. On Avery's medium the pleomorphism was more marked, and smears resembled the direct smears obtained from the original fluid. There was no growth on subculture on plain agar, plain broth, glucose broth and serum inulin water.

Animals were inoculated without producing death. A rabbit was given an intravenous injection of a twenty-four hour culture suspended in salt solution. Death did not occur although several subsequent injections were made. A white mouse was injected intraperitoneally. Instillation of a twenty-four hour growth into the nasal cavity of a guinea-pig to determine whether infection would occur by that route produced no effect.

DISCUSSION

Cellular Content of the Spinal Fluid.—The cell count of the spinal fluid in influenzal meningitis varies, although most observers report the predominance of polymorphonuclear cells. In our case we found 3,400 and 10,000 cells, most of which were polymorphonuclear. Hill's [1] patient had fifty cells, mainly lymphocytes. Davis [2] reported four cases in which turbid fluid was present under high pressure, the polymorphonuclear cells forming from 6 to 80 per cent. of the total count. He

1. Hill: New York M. J. **107**:345, 1918.
2. Davis: Am. J. Dis. Child. **1**:249 (Feb.). 1911.

remarks on the presence of endothelial cells, which we have also found. Boland [3] reports 1,000 cells with 90 per cent. polymorphonuclear cells. The fluid in this case became so thick that it finally failed to pass through the needle. Brown [4] describes the case of a 5 months old infant who had three punctures on successive days. There were 1,600 cells with 96 per cent. polymorphonuclear cells and 3,400 and 3,600 cells the two following days, all of which were polymorphonuclears. He reports another case, an infant, 1 year old, with 6,080 cells, 73 per cent. of which were polymorphonuclears. Ross and Moore's [5] case had 86 per cent. polymorphonuclears, and Moody's [6] 11 months old patient had 256 cells, of which 230 were polymorphonuclears. Another patient, aged 8 months, had 490 cells with 90 per cent. polymorphonuclears. Bhat [7] had a 14 months old infant with 150 cells, of which 54 per cent. were polymorphonuclears and 46 per cent. lymphocytes. There were eighteen endothelial cells for 100 leukocytes. Later punctures showed more polymorphonuclear cells. Stone [8] collects two cases, Hills and his own, which had bloody fluid uniformly.

Blood Count.—Few reports in the literature mention blood counts. In our case there were 7,600 cells of which 72 per cent. were polymorphonuclears, 28 per cent. small mononuclears, 3 per cent. large mononuclears and 1 per cent. transitionals. A normal infant of 17 months averages about 40 per cent. polymorphonuclears and 60 per cent. mononuclears. There appears to be a slight leukopenia in our case although the cell count of the spinal fluid is high and the majority of the cells are polymorphonuclears. The further significance of the leukopenia in influenza is a nonspecific activity of the leukocytes, as demonstrated by Tunnicliff.[9] She states that this decreased activity continues until the patient recovers, in which case the leukocytes become normally active and increase in number. She suggests that leukopenia and diminished phagocytosis may account for the severity and frequency of secondary infections. Hill and Packard [10] state that the blood shows a moderate leukocytosis, usually under 15,000, with an increase in polymorphonuclear cells. Stone had a case in a girl, 15 years old, who had 83 per cent. polymorphonuclear cells. Moody's second patient had 12,300 leukocytes.

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3. Boland: Lancet **2**:704, 1915.
4. Brown: Canad. M. A. J. **5**:1076, 1915.
5. Ross and Moore: Brit. M. J. **2**:1056, 1913.
6. Moody: J. Missouri M. A. **13**:328, 1916.
7. Bhat: Lancet **2**:384, 1917.
8. Stone: Texas State J. M. **15**:318, 1920.
9. Tunnicliff: J. A. M. A. **71**:1733 (Nov. 23) 1918.
10. Hill and Packard: Quoted in Editorial, Lancet **2**:189, 1915.

The Organism in the Spinal Fluid.—The organism found in the spinal fluid has been abundantly described. Pleomorphism in culture and smears from the meninges is its most striking feature. The descriptions are much alike. The bacilli are gram-negative and grow only on blood medium as dew drop transparent colonies. They vary in size from small, plump, coccoid organisms to long thread forms resembling leptothrix with which they have often been confused. Henry [11] states that influenza-like organisms in some cases exhibit bipolar staining which makes them resemble diplococci. He also remarks that sometimes the long forms do not appear for three or four days, while in other cases they appear early. The longer forms often predominate, and the organisms are practically always extracellular. This is probably an indication of diminished phagocytosis. The pleomorphism persists in subcultures on blood agar. Studying the development of pleomorphism, Brown stated that after from fifteen to twenty-four hours, minute regular bacilli appeared, among which threads were seen. On the second day, the curved forms and threads were usually increased, and the bacilli were thicker. Wollstein [12] describes the influenza bacillus as being a slender rod, varying in size, staining deeply at the poles and gram-negative. She emphasizes that the invariable and most prominent characters are, first, hemophilic property and second, pleomorphism. In one of her cases she found long forms with curved ends, often clubbed, corresponding to involution forms found in old cultures and a few characteristic small forms. In two others there were long threads but the typical small forms predominated. Bhat also speaks of long forms which were found end to end by cell membrane and Ager and Avery [13] remarked that the organism from their case exhibited polar staining and varied in size, often occurring in threadlike forms. It has been stated that the chains and convolutions are bacilli placed end to end united by continuation of the cell membrane.

The organism from Moody's second case did not grow on Loeffler's medium.

Ross and Moore isolated the organism from the fluid of the right ventricle.

Following Jordan's [14] observation on indol formation by the influenza bacillus, Rivers [15] found that eleven of twelve cases of influenzal meningitis yielded an indol reaction on the spinal fluid directly.

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11. Henry: J. Path. & Bacteriol. **17**:174, 1912.
12. Wollstein: Am. J. Dis. Child. **1**:42 (Jan.) 1911.
13. Ager and Avery: Arch. Pediat. **27**:284, 1910.
14. Jordan: J. A. M. A. **72**:1542 (May 24) 1919.
15. Rivers: J. A. M. A. **75**:1495 (Nov. 27) 1920.

Its Relation to Pfeiffer's Bacillus.—The pleomorphism of the organism in this type of meningitis raises the question of its classification. Invariably, it is hemoglobinophilic. Its growth is always in the form of dew drop colonies only produced by the influenza bacillus described by Pfeiffer. It is always gram-negative. However, animal inoculations give varying results, and its morphology is somewhat perplexing. There are many who believe that the organism producing meningitis is a bacillus quite distinct from Pfeiffer's bacillus. They insist that this is a pseudo-influenza or an influenzoid organism. Cohen [16] is the chief proponent of this separate organism theory. He states that a septicemic type of influenza bacillus exists which causes meningitis, inasmuch as experimental septicemia cannot be produced, except in those with influenzal meningitis. He concurs with Pfeiffer's original view that the organism does not occur in the blood, but that the meningeal type produces a septicemia in rabbits with serous lesions, as in the human. He has found that vaccination may be carried out against the organism, but the serum of vaccinated animals is neither curative nor preventive, and phagocytic and agglutinative reactions do not distinguish this organism sufficiently from Pfeiffer's bacillus. The differences are summed up in this way by Henry. The organism from meningitis shows bacillary and filamentous forms in culture more readily than does Pfeiffer's organism. It is more readily recovered from heart's blood and tissues than the organism from influenza. It tends to kill laboratory animals by septicemia rather than by toxemia, and fatal results occur with much greater regularity than is the case with Pfeiffer's bacillus.

On the other hand, Wollstein believes that it may be considered as conclusively established that a pseudo-influenza bacillus producing pathologic conditions in human beings as distinct from the true influenza bacillus does not exist. She suggests that the frequent finding of the influenza bacillus in endocarditis, purulent arthritis, empyema, appendicitis, peritonitis, meningitis, otitis, as well as its frequent occurrence in the bronchial and nasopharyngeal secretions in cases of clinical influenza indicates that that organism, like the pneumococcus, is capable of causing inflammations of the serous membranes anywhere in the body. Along these lines Rivers offers the suggestion that the influenza [17] bacillus may be a group of organisms like the streptococcus, which has been divided into hemolytic and nonhemolytic strains and further subdivided by cultural characteristics and serologic tests. He exacts ten requirements for the true influenza bacillus. These tests are hemophilic quality, colony formation, hemolytic test, reaction to Gram's

16. Cohen: Ann. de l'Inst. Past. **23**:273, 1909.
17. Rivers: Bull. Johns Hopkins Hosp. **31**:50, 1920.

stain, morphology, motility, indol formation, found by Jordan to occur in ten of thirteen strains, reduction of nitrates to nitrites, amylase formation and reaction in blood, broth and milk. Further evidence that the meningeal organism is the true influenza bacillus is offered by Slawyk,[18] who isolated a bacillus from the blood and spinal fluid in meningitis which Pfeiffer agreed was the influenza bacillus, and by Thursfield,[19] who found the organism in the blood without meningitis. Flexner [20] interprets the situation by expressing that nearly all cases of influenzal meningitis are examples of bacteremia, since the bacilli are frequently cultivated in large numbers from the blood during life or at necropsy.

To compromise the two views, Henry states that there is a group of hemoglobinophilic organisms causing meningitis whose members range from the influenza bacillus of Pfeiffer which, when it kills, does so by toxemia, to Cohen's organism of very high virulence which kills laboratory animals regularly by septicemia. Ross and Moore state it is impossible to dogmatize whether the organism isolated from sporadic cases of meningitis is identical with the organism in the respiratory tract in influenza. It is sufficient to say that there is a group of cases showing pyemic characters in which meningitis is a common occurrence and in which the only organism present is a hemophilic bacillus having the characteristics of the influenza bacillus. After all these reports and opinions, is it not possible that the influenza bacillus is subject to involutions? The conditions of growth in the spinal canal are somewhat comparable to the conditions in a fluid medium such as Avery's medium. We found that the typical influenza bacilli which were grown by subculture of the pleomorphic bacillus from the spinal fluid on the solid medium of chocolate agar reverted to pleomorphism when grown in Avery's medium.

Animal Inoculation.—The organism in our case was not pathogenic for guinea-pigs, rabbits or mice, despite repeated injection. There are reports of other organisms which illustrate the low pathogenicity we found. Henry injected three rabbits intravenously, intraperitoneally and subcutaneously, respectively, with no illness resulting and no findings when the animals were killed. Ager and Avery failed to produce infection in a guinea-pig inoculated with the organism from their patients, but a rabbit previously bled 15 c.c. died in forty-eight hours. Torrey's [21] organism was of low pathogenicity tested by rabbits. Ritchie's [22] observations differ to this extent. The real influenza bacillus

18. Slawyk: Ztschr. f. Hyg. **32**:443, 1899.
19. Thursfield: Quoted by Rivers, Reference 17.
20. Flexner: J. A. M. A. **57**:16 (July 3) 1911.
21. Torrey: Am. J. M. Sc. **152**:403, 1915.
22. Ritchie: J. Path. & Bacteriol. **14**:615, 1910.

is at first innocuous to guinea-pigs but after subculture for five months it gives a septicemia in guinea-pigs by intraperitoneal injection.

Many observers obtain positive results by animal inoculation. The second generation of the organism from Hill's case inoculated intraperitoneally into a white mouse caused death in less than twenty-four hours. Intravenous injection into a 900 gm. rabbit was followed by death in thirty-six hours, and the organism was recovered from the heart's blood. Wollstein's work in 1911 demonstrated that mice were highly susceptible to small injections intraperitoneally whether the cerebrospinal fluid or pure cultures of the organism were used. Animal passage through mice did not appreciably increase the virulence, although only one half the dose was required to kill after passage.

Guinea-pigs died in from twelve to twenty-six hours after injection of from one-half to whole cultures. Rarely was phagocytosis found, although there were polymorphonuclear cells in the peritoneum. Sometimes, the animals lived for three or four days.

Rabbits injected with twenty-four hour cultures died in from fifteen to thirty-six hours, and the bacilli were recovered from the mucosal surface of the upper nasal cavities.

Monkeys injected subdurally by spinal puncture yielded symptoms in from six to twelve hours.

Wollstein found that out of a large number of strains, four were found to be virulent for rabbits. Three of these were obtained from influenzal meningitis spinal fluid. Many necropsies were examined for bacilli from the blood without results. She states that the bacilli are more frequently isolated from the blood postmortem in the cases of meningitis. All strains were found virulent for small animals. In general, the high virulence for human beings ran parallel with the effects on rabbits and monkeys.

Albert and Kelman [23] find that the bacilli are usually destroyed rapidly after their introduction into the body, but following intraperitoneal injections, the organism may appear in the blood. They also state that the bacillus produces a toxin which is fatal to mice, guinea-pigs and rabbits almost as soon as broth cultures. Death occurs in from one and one-half hours to thirty days after injection. They suggest that death occurring after four days may be caused by secondary invading organisms. It is their experience that guinea-pigs are more uniformly susceptible than rabbits or mice, and rabbits show a greater individual variation in susceptibility. On the basis of their work, they conclude that the influenza bacillus is distinctly pathogenic to mice, guinea-pigs and rabbits, but that this quality is apparently limited to certain cultures or strains of the organism.

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23. Albert and Kelman: J. Infect. Dis. **25**:433, 1919.

PATHOGENESIS

The influenza bacillus behaves like the pneumococcus. It has been found in the mouth in 43 per cent. of persons [24] examined. Considering the upper respiratory tract as the most frequent portal of entry, Wollstein explains the localization of the organism in the middle ear, bronchi and lungs. In Brown's case of a 5 months' old infant there was double otitis media with preceding bronchitis, in which the influenza bacillus was found in pure culture. The blood, nasopharyngeal and postmortem culture of brain, heart's blood, lung and mastoid all yielded the organism. This well illustrates the belief of Wollstein that the influenza bacillus acts like the pneumococcus and is equally as capable of producing inflammations of the serous membranes anywhere in the body.

To determine the rôle of the upper respiratory tract in the etiology of influenzal infections Bloomfield [25] introduced the organism into the upper respiratory passages. Several strains so introduced disappeared in from one to three days. No carrier states were produced, and no local or general pathologic processes resulted from the inoculation. Bacilli isolated more than twenty-four hours after introduction were shown to be different strains, and they were not viable after suspension in saliva for twenty-four hours at 37 degrees C.

The middle ear undoubtedly plays an important rôle in the development of influenzal meningitis in children. Ritchie quotes Kossel as finding in 108 postmortem examinations in children under 1 year of age, eighty-five cases of otitis media, over half of which were of influenzal meningitis. Hartman and Honel [26] have found 90 per cent. of cases of otitis media in infants of influenzal origin. Our case may have been one of influenzal otitis media originally although late cultures showed staphylococci which may have been secondary invaders. Suppuration of the frontal and maxillary sinuses was the source of infection in Torrey's first case. Henry states that infection may come directly through the carious bone or by blood vessels running through the remains of the petrosal squamosal suture from the antrum to the middle fossa without direct extension or caries. The nasopharynx, he suggests, may be the portal through which the bacilli are conveyed by the nasal lymphatics to the anterior fossa of the skull, through the cribriform plate of the ethmoid.

Opinion seems to favor a bacteriemia as the mechanism in the production of meningitis, although this cannot always be demonstrated. Inoculation of the bacilli intravenously in rabbits has resulted in positive blood culture postmortem. Following intraperitoneal injection they

24. Pritchell and Stillman: J. Exper. M. **29**:259, 1919.
25. Bloomfield: Bull. Johns Hopkins Hosp. **31**:85, 1920.
26. Hartman and Honel: Quoted by Henry, Reference 11.

may appear in the blood, probably depending on the virulence of the organism and the lowered resistance on the part of the body.[23] After subdural inoculation, they may be recovered from the upper nasal mucosa, suggesting that they are excreted at this point.[13] Since they also reach the blood, they may be secreted from the blood and not directly through the meninges. After intravenous injection of influenza bacilli into rabbits they are found in the secretions of the mucosa. They are excreted by the kidneys in rabbits and guinea-pigs, and pure cultures may be obtained from the surface of the cord and brain in rabbits and guinea-pigs inoculated intravenously or intraperitoneally, although no lesions or inflammations of the meninges are found. From this experimental evidence, Wollstein believes that the bacilli may be present in the spinal fluid without causing meningitis and permitting a clear fluid.

In furtherance of the theory of bacteremic pathogenesis of influenzal meningitis, Henry thinks that the occurrence of bronchopneumonia, pleurisy and pericardial inflammations, complicated with meningitis, allows the assumption that the bacilli are carried to the meninges by the blood stream or pass to the cervical meninges by the thoracic lymphatics, as in some cases of tuberculous meningitis. It will be remembered that Flexner stated that nearly all cases of influenzal meningitis are examples of bacteriemia, as demonstrated by the frequent positive blood findings during life or at necropsy. Davis states that the meningeal infection is probably hematogenous in origin, even though the heart's blood cultures after death may be negative. Difficulties encountered in making blood cultures in young children during life are responsible for the absence of data on this point, but we can say that in the majority of the fatal cases of influenzal meningitis a general blood infection occurs whether this invasion is primary or secondary.

PROGNOSIS

More cases of influenzal meningitis occur in infants and young children than in adults, and the process is more severe in children. Stone collected 105 cases, with a mortality of 91.4 per cent., nine patients recovering.

TREATMENT

To reduce the high mortality many agencies have been tried. From the medicinal standpoint, hexamethylenetetramin, in 10 grains doses, at four hour intervals was followed by improvement in one case reported by Ross and Moore although the final outcome is not reported.

The diminished phagocytosis in influenzal infections suggests that favorable results may be obtained by measures aimed to increase leukocytic activity. Practically no phagocytosis occurs, as is evidenced by

the extracellular arrangement of the organism in the spinal fluid. In fact, there seems to be evidence for Torrey's contention that protective substances may pass out into the spinal fluid following spinal puncture due to lowered pressure and consequent increased outpouring into the cerebrospinal space. Following lumbar puncture, there is increased phagocytosis and decrease in the organism. In one of Torrey's cases, the organism became intracellular at the second puncture. The good effect following tapping, he states, may also be due to relief of high pressure, improved blood supply, and removal of toxins.

Spinal lavage in Ross and Moore's case resulted in a less involved spinal cord than brain.

Regarding specific therapy, Cohen states that animals may be vaccinated against the organism, but that the serum of vaccinated animals is neither curative nor preventive. Tunnicliff suggests that convalescent serum or immune horse serum may promote leukocytosis and increase antibody content of the serum. In this connection Johnson [27] reports the case of a 3 year old boy who recovered following the injection of convalescent serum intraspinally and subcutaneously. It is to be expected that normal serum may increase phagocytosis and improve the condition.

CONCLUSIONS

1. Influenzal meningitis is accompanied by a widespread distribution of the influenza bacillus in the upper respiratory tract.

2. The organism is easily cultivated from the spinal fluid and in many cases from the blood.

3. The organism from the spinal fluid is usually pleomorphic, showing many long thread forms.

4. It seems plausible that the pleomorphism is but a minor variation from the so-called typical influenza bacillus, and that this may be due to the peculiar conditions of its habitat.

5. Spinal fluid usually contains a large number of polymorphonuclear cells which show no tendency to phagocytosis.

6. The blood count does not give the typical leukopenia of respiratory influenza.

7. Animals show a variable response to injections of the organism, although the bacillus is usually pathogenic for laboratory animals.

8. Prognosis of influenzal meningitis is very grave.

9. The most rational treatment at the present time is the administration of convalescent or normal serum and frequent removal of spinal fluid. The serum contains antibodies and promotes phagocytosis, and spinal puncture removes fluid and increases phagocytosis.

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27. Johnson: Arch. Pediat. **36**:82, 1919.

A PRELIMINARY REPORT OF THE STUDY OF BREAST FEEDING IN MINNEAPOLIS *

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Most of the members of this organization have heard me in season and out of season, talking about breast feeding, and the study we have been making of it at the University of Minnesota. Although the statistics will not be ready until September, enough data have come so that we have records which indicate what we have learned and accomplished. I have had so many inquiries in regard to our technic, that I am taking this opportunity to explain the essential parts to those who are interested.

The investigation of breast feeding in Minneapolis was planned to study the wider applicability of certain principles of breast feeding which we have been using at the University of Minnesota and in private work. We wished to see whether these principles are applicable to a wider field, and to all strata of society. We wished to make a statistical study to observe the effect, if any, on infant mortality. Dr. Rood Taylor made a study of the records of our New-born Clinic at the University recently and he found that in one thousand consecutive cases in which the mother and the baby left the hospital together each child was at the breast. This disposes of the importance of the bogey, agalactia. The idea that the mothers often have no milk for their new-born babies was not given much consideration in this study. The technic of the maintenance and reestablishment of breast feeding is that which I described in my chairman's address in New York in 1917 [1] and I shall mention simply the essentials here.

The demand which is made on the breast is by far the most important factor in the maintenance of the breast milk supply. Repeated, regular and complete evacuation of the breasts by a vigorous baby, is, of course, the natural and best method. When this natural stimulus is not obtained or when the demand on the breast is insufficient for any reason, the supply of breast milk dwindles gradually until the breast does not support the baby. In these cases artificial aid is

* Received for publication, Dec. 8, 1920.
* Read before the American Pediatric Society, June, 1920.

1. Establishment, Maintenance and Reinstitution of Breast Feeding, J. A. M. A. **64**:417 (Aug. 11) 1917.

necessary. In an interesting paper published in 1913, Zlocisti showed that this can be accomplished by putting the father at the breast, and stimulating the lactation systematically. This, however, is open to many esthetic and social objections. We have found that in most cases, using the principle of stimulation but by milking the breast, we are able to accomplish a similar or even better result. A cross section of the breast shows that the milk sinuses are largely just back of or in the area under the colored areola. The gland proper is farther back. We apply the same principles that the milkmaid applies. She does not stroke the cow's udder. She grasps the teats only. We do not massage or stroke the breasts over the glandular tissue as this often causes injury. We grasp the breast just back of the colored areola, press the forefinger and thumb together, thus closing off the sinuses. Then, using a milking motion, push forward then outward, thus emptying the ducts and sinuses to the nipple itself. This should be done gently and should not be painful. No trauma should be done the nipple and the gland tissue of the breast itself is not injured.

Let us consider the premature baby first. Many a premature baby has been deprived of its mother's breast milk unnecessarily. The milk of the mother of the premature baby dries up, not because of the baby being born prematurely, but because the premature baby cannot make the proper demand on the breast. We make the practice of milking the mothers breasts as described above, and giving the milk to the premature baby, usually by means of a tube. In our experience these mothers of premature babies furnish milk just as well as mothers of full time babies, and in case after case we have found that these mothers who are milking their breasts, and not laying the baby on the breast on account of the weakness of the baby, have just as good a milk supply, and often are able to furnish milk for their own babies and for another baby besides. When we have intelligent mothers who cooperate well we do not at all feel that the breast feeding of the premature baby is difficult.

It may take a little more time but the mothers are almost always sympathetic and willing to aid in this work and do not complain of the extra time involved. Most of our premature babies are fed with a tube for a month or two before they are laid at the breast at all. It is certainly much less trouble than wet nursing.

It is not only in cases of prematurity that this method is of value for keeping the breast milk up. When a baby is weak from any cause, or ill, so as not to be with the mother, or even when the mother is required to be away for a period, as in one case for two weeks, this method will keep the supply up.

When the trouble is with the breast or the nipple itself, this

method may be used to advantage. In one case a mother had failed to nurse two children because of a badly inverted nipple on one side. With the third lactation she was shown how to express the milk and encouraged in carrying out this procedure over a long period. At the end of nine months, she was nursing the baby at one breast fully and on the other she had expressed the milk at every feeding; five times in every twenty-four hours during the whole nine months period. When she appeared for the weaning of the baby, at the end of nine months she was getting more milk from the breast on which she could not lay the baby, and from which she had expressed the milk regularly, thus furnishing the stimulation artificially, than she was getting from the breast on which the baby was being laid. In cases in which the nipple is sore or where there is a fissure, this method can be used to let the nipple have the proper rest, and at the same time the breast milk is not lost for want of stimulation. Expression can be used without any injury to the nipple itself. It would be a mistake to leave the impression that we depend wholly on expression in this study of breast feeding. Every other method of encouraging and instructing the mothers in breast feeding is applied also. Expression is reserved largely for the more difficult cases. However, I wish to stress the demand made on the breast and the expression as the important means, rather than the very common giving of enormous quantities of fluid. We know enough now about the physiology of the breast, if we could apply it, to get at least 90 or 95 per cent. of the babies nursed at the breast.

In organizing the bureau for carrying on this study, we began with the medical men. We wrote to every physician in the city announcing the formation of the bureau, we invited them to meet at the University, and explained the purpose; we sent representatives to talk with them and explain all details. We made it quite plain that no physician in active practice would be employed in connection with the work. I was fortunate in that I was confining my private work to consultation and referred work. Each physician was asked for criticisms. A card index of the physicians was maintained on which any special desire of the physicians was recorded. In most cases the physicians wished that we go directly into the cases, but report to them afterward. Some wished, however, to have us report to them before going in. Some wished all our statements and directions to come through them personally. We respected all these wishes. After we had been in operation some time, we sent a representative to all the physicians again to ask whether we were embarrassing them in any way, and asked for suggestions to prevent such embarrassment. The Minneapolis Health Department cooperated in every way possible; not

only passively but actively. The Infant Welfare Society took up the work of getting information for us from the families with whom they were working. Prominent citizens and the daily papers participated and aided in many ways.

The Breast Feeding Investigation Bureau of the Department of Pediatrics of the University of Minnesota was the name under which the work was carried on. The graduate school of the University appropriated $1,000 for the study. The war chest appropriated $3,000. From private individuals and other sources, about $1,500 more was paid, thus making the total amount between five and six thousand dollars for the year's study.

The mother of practically every baby born in Minneapolis during the year was followed for nine months. The birth reports were sent in from the health department every day, and the first information concerning the breast feeding was obtained by telephone or personal call. If things were going well literature was sent each month. If the return cards were not sent back, the case was followed up by telephone or personal call. If there was any trouble with the breast feeding, the bureau was thus informed and the doctor was consulted, a nurse sent out to instruct the mother when necessary, even daily. The literature was as follows:

1. Is your baby being breast fed?.....
2. If not, when and why did you stop?.....
3. How many other children have you had?.....
4. Give years of births: 1..... 2..... 3..... 4.....
5. How many are living?.....
6. If you have lost any, at what ages and from what cause?.....
   .....
7. How long was each child at the breast only? (If but a few days or short time, state as nearly as possible the number of days.)
   1..... 2..... 3..... 4.....
8. When was the breast stopped in each case?
   (1).....mos. (2).....mos. (3).....mos. (4).....mos.
9. Give reason for stopping breast feeding in each case if before the ninth month.
   1..... 2..... 3..... 4.....
10. If bottle was given with the breast, when was it begun and was it in addition to each breast feeding or in place of certain breast feedings.
    1..... 2..... 3..... 4.....
    I can be reached by Phone No.....

POST CARD

DEAR MADAM:

Summer will soon be here. It is especially important now for your baby to be kept upon the breast. There is much more danger for the bottle-fed baby when the weather is hot.

We wish to make sure again that you have no difficulty with the breast feeding which can be prevented.

We are, therefore, taking the liberty of sending you another card, asking you to answer the following questions and return it to us.

Thank you.

For THE BREAST FEEDING INVESTIGATION BUREAU.

.....

(1) Is your baby still breast-fed?.....
(2) How often do you feed it?.....
(3) Does it receive the breast only?.....
(4) Are you having any difficulty nursing the baby?.....
.....
(5) If so, what?.....
(6) If not breast-fed, when and why did you stop? (State how long the baby was breast-fed.) .....
.....

POST CARD

(1) Is your baby still breast-fed?.....
(2) How often do you feed it?.....
(3) Does it receive the breast only?.....
(4) Are you having any difficulty nursing the baby?.....
.....
(5) If so, what?.....
(6) If not breast-fed, when and why did you stop? (State how long the baby was breast-fed.) .....
.....
.....
.....
Have you or the baby had influenza?.....
Have you a telephone?.....

A report was obtained concerning each child every month.

Such work is usually done in clinics and hospitals, but we reached everybody, rich and poor. We were told, and we also feared, that we would have great difficulty in the private families where the physicians were in charge. This, however, we found not to be true. In almost every case the physician was sympathetic and aided us. When our agents found that there was difficulty with breast feeding we often asked the physician to give us his support, which he almost always did. Many of our workers have reported that they had even less trouble with those who were educated and had means to pay for services of their own physicians and nurses.

Jan. 1, 1920, this work was turned over to the Infant Welfare Society of Minneapolis, thus making it permanent. The final report cannot be given out until nine months after January 1, as babies born in December, 1919, will not be nine months old until September, 1920. The Infant Welfare Society is giving us reports to complete our records.

I would, however, call your attention to the beginning of the report where the total results of the investigation for January, February, March, April and May are listed. The results by months run from 96 per cent. at the end of the second month to 72 per cent. at the end of the ninth month.

TABLE 1.—Total Result of Investigation of Breast Feeding of the January, February, March, April and May Babies Born in Minneapolis During 1919

	Breast Fed		Percentage on Artificial Food
	Number	Per Cent.	
Of the 2,022 babies still under observation at the end of the ninth month	1,472	72+	27+
Of the 2,113 babies still under observation at the end of the eighth month	1,631	77+	22+
Of the 2,240 babies still under observation at the end of the seventh month	1,810	80+	19+
Of the 2,355 babies still under observation at the end of the sixth month	1,992	84+	15+
Of the 2,412 babies still under observation at the end of the fifth month	2,090	86+	13+
Of the 2,505 babies still under observation at the end of the fourth month	2,250	89+	10+
Of the 2,674 babies still under observation at the end of the third month	2,492	93+	6+
Of the 2,847 babies still under observation at the end of the second month	2,761	96+	3+

TABLE 2.—January, 1919, Cases

Six hundred and thirty-six babies were born in Minneapolis during January, 1919. Of these, at the end of each month listed, the data are shown.

	Jan. 31, 1919	Feb. 28, 1919	March 31, 1919	April 30, 1919	May 31, 1919	June 30, 1919	July 31, 1919	Aug. 31, 1919	Sept. 30, 1919
Breast fed	516	486	427	590	345	301	224	146	88
Breast fed complemental*	33	41	67	66	75	94	138	198	242
Total breast fed†	549	527	491	656	420	395	362	344	330
Artificially fed	...	8	24	39	56	80	70	75	85
Total under observation‡	549	535	518	495	476	455	432	419	415
Artificially fed from birth	13	13	13	13	13	13	13	13	13
Baby died	18	21	25	27	28	29	29	31	31
Mother died	3	3	3	3	3	3	3	3	3
Refused to give information	0	3	3	5	5	6	7	7	7
Moved out of town	2	6	13	23	31	40	46	48	49
Cannot be traced	11	15	21	30	40	50	66	75	78
Out of town cases	40	40	40	40	40	40	40	40	40
	636	636	636	636	636	636	636	636	636

RESULT

	Breast Fed		Percentage on Artificial Food
	Number	Per Cent.	
Of the 415 January babies still under observation Sept. 30, 1919	330	79+	20+
Of the 419 January babies still under observation Aug. 31, 1919	344	82+	17+
Of the 432 January babies still under observation July 31, 1919	362	83+	16+
Of the 455 January babies still under observation June 30, 1919	395	86+	13+
Of the 476 January babies still under observation May 31, 1919	420	88+	10+
Of the 495 January babies still under observation April 30, 1919	456	92+	7+
Of the 518 January babies still under observation March 31, 1919	494	95+	4+
Of the 535 January babies still under observation Feb. 28, 1919	527	98+	1+

* By "complemental" is meant breast fed with an addition of some artificial mixture after the breast feeding.

† Sixty-seven mothers of January babies were taught expression of milk from the breasts in order to stimulate the breasts and thereby increase the milk supply.

‡ Jan. 31, 1919, we had 549 of the babies born in January under observation. Sept. 30, 1919, we had 415 of these babies still under observation, 134 of the 549 babies under observation on Jan. 31, 1919, having been dropped for the following reasons: baby died, 13 cases; refused to give information, 7 cases; moved out of town, 47 cases; cannot be traced, 67 cases.

TABLE 3.—FEBRUARY, 1919, CASES

Six hundred and twenty-one babies were born in Minneapolis during February, 1919. Of these, at the end of each month listed, the data are presented.

	Feb. 18, 1919	March 31, 1919	April 30, 1919	May 31, 1919	June 30, 1919	July 31, 1919	Aug. 31, 1919	Sept. 30, 1919	Oct. 31, 1919
Breast fed	520	493	418	362	326	260	188	116	77
Breast fed complemental	31	46	61	63	78	126	168	215	224
Total breast fed*	551	539	479	425	404	386	356	331	301
Artificially fed	...	4	21	38	44	57	77	88	91
Total under observation†	551	543	500	463	448	443	433	419	392
Artificially fed from birth	11	11	11	11	11	11	11	11	11
Baby died	20	23	23	24	25	26	28	28	28
Mother died	1	1	3	3	3	3	3	3	3
Refused to give information	0	0	1	1	1	2	2	2	2
Moved out of town	0	3	19	39	39	40	41	45	54
Cannot be traced	4	6	30	46	60	62	69	79	97
Out of town cases	34	34	24	34	34	34	34	34	34
	621	621	621	621	621	621	621	621	621

RESULT

	Breast Fed		Percentage on Artificial Food
	Number	Per Cent.	
Of the 392 February babies still under observation Oct. 31, 1919	301	77+	22+
Of the 419 February babies still under observation Sept. 30, 1919	331	78+	21+
Of the 433 February babies still under observation Aug. 31, 1919	356	82+	17+
Of the 443 February babies still under observation July 31, 1919	386	87+	12+
Of the 448 February babies still under observation June 30, 1919	404	90+	9+
Of the 463 February babies still under observation May 31, 1919	425	91+	7+
Of the 500 February babies still under observation April 30, 1919	479	95+	4+
Of the 543 February babies still under observation March 31, 1919	539	99+	¼+

* Fifty-four mothers of February babies were taught expression of milk from the breasts in order to stimulate the breasts and thereby increase the milk supply.

† Feb. 28, 1919, 551 of the babies born in February were under observation. Oct. 31, 1919, 392 of these babiees were still under observation, 159 of the 551 babies under observation Feb. 28, 1919, having been dropped for the following reasons: baby died, 8 cases; mother died, 2 cases; refused to give information, 2 cases; moved out of town, 54 cases; cannot be traced, 93 cases.

The cold figures are lifeless but, of course, necessary. I have often thought of it in comparison with our judgment of certain therapeutic procedures. The statistics of the effect of diphtheria antitoxin are of interest and, of course, are also necessary, but each of us has seen the brilliant effect of the administration of the serum in the individual cases which appeals to us more. I remember the enthusiasm of my father, who practiced medicine during the time of the introduction of antitoxin. In like manner our workers became enthused over the fine results in the individual cases. We find that many of them

who could not well afford it were willing to do this work for less pay because of the remarkable results that they saw before them. One of the members of this society once heard me discussing this subject. He evinced some interest and some mental reserve. Later he came out to see us and I sent him out into the field with a nurse, keeping away myself. He saw two cases and ceased to be skeptical about maintenance of breast feeding and was wholly convinced and enthusiastic.

We wish now to supplement this study with one of rural conditions in the state.

Through the members of our staff who are sent out on our rural clinics, we get reports from certain districts in which rickets is very

TABLE 4.—MARCH, 1919, CASES

Seven hundred and ninety-nine babies born in Minneapolis during March, 1919. Of these, at the end of each month listed, the data are presented.

	March 31, 1919	April 30, 1919	May 31, 1919	June 30, 1919	July 31, 1919	Aug. 31, 1919	Sept. 30, 1919	Oct. 31, 1919	Nov. 30, 1919
Breast fed	615	541	470	429	377	339	234	130	62
Breast fed complemental	30	52	78	74	88	115	181	261	273
Total breast fed*	645	593	548	503	465	454	415	391	335
Artificially fed	...	41	58	74	87	96	102	119	132
Total under observation†	645	634	606	577	552	550	517	510	467
Artificially fed from birth	25	25	25	25	25	25	25	25	25
Baby died	20	29	30	32	32	32	35	35	35
Mother died	5	5	5	5	5	5	5	5	5
Refused to give information	1	1	1	1	1	1	1	1	1
Moved out of town	15	16	25	39	49	50	62	67	90
Cannot be traced	25	26	44	57	72	73	91	93	113
Out of town cases	63	63	63	63	63	63	63	63	63
	799	799	799	799	799	799	799	799	799

RESULT

	Breast Fed		Percentage on Artificial Food
	Number	Per Cent.	
Of the 467 March babies still under observation November 30, 1919	335	71+	28+
Of the 510 March babies still under observation Oct. 31, 1919	391	76+	23+
Of the 517 March babies still under observation Sept. 30, 1919	415	80+	19+
Of the 550 March babies still under observation Aug. 31, 1919	454	82+	17+
Of the 552 March babies still under observation July 31, 1919	465	84+	15+
Of the 577 March babies still under observation June 30, 1919	503	87+	12+
Of the 606 March babies still under observation May 31, 1919	548	90+	9+
Of the 643 March babies still under observation April 30, 1919	593	93+	6+

* Eighty-three mothers of March babies were given special attention and taught expression of milk from the breasts in order to stimulate the breasts and thereby increase the milk supply.

† March 31, 1919, 645 of the babies born in March were under observation. Nov. 30, 1919, 467 of these babies still were under observation, 178 of the 645 babies under observation March 31, 1919, having been dropped for the following reasons: baby died, 15 cases; moved out of town, 75 cases; cannot be traced, 88 cases.

common. In these neighborhoods infants are weaned for insufficient reasons. Fortunately, most of the children in the territory covered by our rural clinics, are breast fed. The study of breast feeding in smaller towns and rural districts should be very interesting, and should be made through the physicians as in Minneapolis. The conditions in certain other cities of large and smaller size and the same size over the country should be determined. Minneapolis has a low infant mortality for a city of its size. However, for the first year of the application of this work, the mortality dropped definitely. This may be entirely coincident, but I do not believe that it is.

TABLE 5.—APRIL, 1919, CASES

Seven hundred and nineteen babies born in Minneapolis during April, 1919. Of these, at the end of each month listed, the data are given.

	April 30, 1919	May 31, 1919	June 30, 1919	July 31, 1919	Aug. 31, 1919	Sept. 30, 1919	Oct. 31, 1919	Nov. 30, 1919	Dec. 31, 1919
Breast fed	599	573	486	436	386	312	185	93	35
Breast fed complemental	17	27	56	70	93	134	225	221	224
Total breast fed*	616	600	542	506	479	446	410	314	259
Artificially fed	...	8	22	30	47	60	74	89	128
Total under observation†	616	608	564	536	526	506	484	403	387
Artificially fed from birth	7	7	7	7	7	7	7	7	7
Baby died	19	25	25	26	27	27	28	28	29
Mother died	1	1	2	2	2	2	2	2	2
Refused to give information	0	0	0	0	0	0	0	0	0
Moved out of town	8	9	35	48	53	62	67	70	71
Cannot be traced	15	16	33	47	51	62	77	155	169
Out of town cases	53	53	53	53	53	53	53	53	53
	719	719	719	719	719	719	719	719	719

RESULT

	Breast Fed		Percentage on Artificial Food
	Number	Per Cent.	
Of the 387 April babies still under observation Dec. 31, 1919	259	66+	33+
Of the 403 April babies still under observation Nov. 30, 1919	314	77+	22+
Of the 484 April babies still under observation Oct. 31, 1919	410	84+	15+
Of the 506 April babies still under observation Sept. 30, 1919	446	88+	11+
Of the 526 April babies still under observation Aug. 31, 1919	479	91+	8+
Of the 536 April babies still under observation July 31, 1919	506	94+	5+
Of the 564 April babies still under observation June 30, 1919	542	96+	3+
Of the 608 April babies still under observation May 31, 1919	600	98+	1+

* Sixty mothers of April babies were taught expression of milk from the breast in order to stimulate the breasts and thereby increase the milk supply.

† April 30, 1919, we had 616 of the babies born in April under observation. Dec. 31, 1919, we had 387 of these babies still under observation, 229 of the 616 babies under observation April 30, 1919, having been dropped for the following reasons: baby died, 10 cases; mother died, 2 cases; moved out of town, 63 cases; cannot be traced, 154 cases.

TABLE 6.—MAY, 1919, CASES

Six hundred and fifty-seven babies born in Minneapolis during May, 1919. Of these, at the end of each month listed, the data are shown.

	May 31, 1919	June 30, 1919	July 31, 1919	Aug. 31, 1919	Sept. 30, 1919	Oct. 31, 1919	Nov. 30, 1919	Dec. 31, 1919	Jan. 31, 1920
Breast fed	506	446	363	301	266	221	164	87	66
Breast fed complemental	32	56	66	59	56	90	103	164	181
Total breast fed*	538	502	429	360	322	311	267	251	247
Artificially fed	...	16	54	74	88	90	107	111	114
Total under observation†	538	518	483	434	410	401	374	362	361
Artificially fed from birth	11	11	11	11	11	11	11	11	11
Baby died	17	22	22	24	24	25	26	26	26
Mother died	2	2	2	2	2	2	2	2	2
Refused to give information	0	0	0	0	0	0	0	0	0
Moved out of town	7	9	19	32	53	56	56	59	59
Cannot be traced	30	43	68	102	105	110	136	145	146
Out of town cases	52	52	52	52	52	52	52	52	52
	657	657	657	657	657	657	657	657	657

RESULT

	Breast Fed		Percentage on Artificial Food
	Number	Per Cent.	
Of the 361 May babies still under observation Jan. 31, 1920	247	68+	31+
Of the 362 May babies still under observation Dec. 31, 1919	251	69+	30+
Of the 374 May babies still under observation Nov. 30, 1919	267	71+	28+
Of the 401 May babies still under observation Oct. 31, 1919	311	77+	22+
Of the 410 May babies still under observation Sept. 30, 1919	322	78+	21+
Of the 434 May babies still under observation Aug. 31, 1919	360	82+	17+
Of the 483 May babies still under observation July 31, 1919	429	88+	11+
Of the 518 May babies still under observation June 30, 1919	502	96+	3+

* Forty-five mothers of May babies were taught expression of milk from the breasts in order to stimulate the breasts and thereby increase the milk supply.

† May 31, 1919, 538 of the babies born in May were under observation. Jan. 31, 1920, 361 of these babies still were under observation, 177 of the 538 babies under observation May 31, 1919, having been dropped for the following reasons: baby died, 9 cases; mother died, 52 cases; cannot be traced, 116 cases.

TOXIC SYMPTOMS IN INFANTS AND CHILDREN WITH GASTRO-INTESTINAL MANIFESTATIONS.*

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Severe toxic symptoms have long been described in infants who are suffering from various intestinal conditions, but the peculiar group of symptoms to be discussed in this article have been brought to the notice of pediatrists very forcibly by Finkelstein and termed by him "alimentary intoxication." Of late, others have grouped these cases under the term "acidosis." Finkelstein's alimentary origin of this condition has not by any means been proven, and as to the acidosis, we have seen many patients who had no diminished carbon dioxid in the blood. This latter fact has been noted by Schloss [1] and others. We have, therefore, been most careful in the selection of our title, for even the intestinal origin of this condition has not been proven.

The symptom complex is always associated with gastro-intestinal symptoms, and seems to occur almost wholly in the summer months, seen in our hospital wards from July to September, and most frequently during July and August. It does not seem to be much more prevalent during extremely hot summers and does not resemble the cases of heat stroke in infants. Males and females are equally affected. Prematures, or those congenitally weak, seem more prone to this condition than the strong and vigorous, for five out of our series of twenty-three cases were in prematures. It is relatively rare in children when the hygiene and living conditions are good, for we have never seen it occur in the better class of private practice. It is, perhaps, less common in very early infancy, occurring infrequently before the fourth month and most often between the sixth and tenth months. This may be due firstly, to the fact that usually more than one gastro-intestinal upset has occurred before the toxic symptoms supervene, and secondly, that the purely breast fed infant is almost immune from this condition. The age incidence is rather in contradiction to Ylppo [2] who seems to think that the new-born has a predilection to acidotic conditions. Yet Seham [3] was unable to confirm this. In

* Received for publication, Dec. 22, 1920.

* From the Pediatric Service and Pathological Laboratory, Department of Physiological Chemistry, Mt. Sinai Hospital.

1. Schloss, O., and Stetson, R. E.: Am. J. Dis. Child. **13**:218 (Feb.) 1917; Schloss, O.: Am. J. Dis. Child. **15**:165 (Feb.) 1918.
2. Ylppo, A.: Ztschr. f. Kinderh. **14**:268, 1916.
3. Seham, M.: Am. J. Dis. Child. **18**:42 (July) 1919.

our series, all subjects, but one, were in babies artificially fed. This one was an infant, aged 6 weeks, born congenitally weak, and much under weight.

In many instances there was a history of difficult feeding and numerous attacks of diarrhea, yet in some of our cases the history was relatively free from intestinal upsets and the child was doing perfectly well on its formula.

However, in every case gastro-intestinal symptoms were present or had been present before the toxic symptoms occurred. Usually, the child began with an ordinary diarrhea, with a few lumpy and loose movements. This continued either for a few days or a few weeks before vomiting began. At times vomiting and diarrhea began almost simultaneously, the stools becoming gradually more and more frequent and the vomiting persisting. The toxic symptoms usually began a few days or even weeks after the onset of the diarrhea. These were ushered in by restlessness and irritability and followed by apathy, semi-coma and coma.

The children present a picture of being acutely and seriously ill. The skin has an ashen gray, slightly cyanotic appearance, hangs in folds, later frequently becoming scleremic. The fontanel is sunken, upper lids falling over the eyeball, at times resembling a complete ptosis. The cornea is dry and in young infants the iris changes from its characteristic light blue to a brownish gray.[4] The tongue and the mucous membranes of the mouth have a reddish hue.

The respirations in some cases are apparently normal. In others, they are rapid and shallow, and in still others there is present the typical hyperpnea or deep breathing so frequently described. The rapid respirations may be present without any physical or roentgen signs of pneumonia and hyperpnea present or absent, with or without a low carbon dioxid content of the blood. In some cases there may be a complicating pneumonia, but this is not usual. In our cases it was interesting to note how negative the physical examinations were. The heart rarely presented any adventitious sounds. The electrocardiograph was usually normal showing only an occasional tachycardia. The spleen was rarely palpable and the liver was only moderately enlarged.

The nervous system was markedly affected—irritability, then apathy, finally coma and unconsciousness being the rule. Convulsions were not frequent, and if present they were usually terminal. No abnormal reflexes were noted.

Fever was present in most of the cases. It was very irregular and often very high, extending over many days, although absolutely

4. Schindler, E.: Ztschr. f. Kinderh. **19**:153, 1919.

no physical signs could be elicited in the way of complications referable to the ear, lungs or the pelvis of the kidney. The temperature was not influenced by the withdrawing of food nor was it lowered by the administration of fluids. Many of the terminal temperatures were very high, reaching 106 F. In a few cases observed only a few hours or days, in which the entire history was very short, there was a subnormal temperature.

The vomiting was usually most persistent and occurred with any form, kind and quantity of food given. The vomiting usually consisted of the ingested food; blood was never seen. Gavage and lavage were of no avail.

The stools were either very watery and frequent, or full of mucus and green; although it was not unusual to have them become almost normal in color and consistency and yet the toxic symptoms continue. Blood was not often present.

The urine was reduced in amount in every case—more than could be accounted for by the diarrhea and vomiting. Even after many subcutaneous and peritoneal injections the quantity excreted was very small. It seemed to us that the quantity of urine excreted was often directly proportionate to the severity of the symptoms, yet there seemed to be no direct relation between the quantity excreted and the blood findings. We hope that during the next summer we shall be able to report more accurately on twenty-four hour quantities in these cases. The specific gravity was usually high and albumin and casts were found in most cases. Sugar (Fehlings), acetone and diacetic acid were present at times, often, however, they were absent, regardless of the amount of voluntary and involuntary starvation and the severity of the symptoms. Excessive amounts of uric acid and ammonium urate crystals [5] were found in a few cases and are thought by some to signify a bad prognosis. Indican was present in considerable quantity in some cases. The percentage of ethereal sulphate to total sulphates was greatly increased in three cases examined. The kidneys in one case, in which there was almost complete anuria and high retention of nitrogen in the blood, were examined histologically (Dr. Baehr) and found to be practically normal. In this same case the liver was fatty, and there was a marked congestion of the gut.

The duration of this condition varies; at times it is very virulent and lasts but a few days; again, it may last from three to four weeks with periods of marked improvement.

The prognosis is bad; nineteen out of twenty-three patients died (87.5 per cent.). This agrees with Schloss, Hamburger [6] and others.

5. Morgenstern, K.: Ztschr. f. Kinderh. **19**:129, 1919.
6. Hamburger, R.: Jahrb. f. Kinderh. **93**:25, 1920.

Analysis of Blood and Urine of Cases of Toxic Symptoms Occurring in Infants and Children

No.	Age in Mos.	Sex	Days Sick in Home	Days Sick in Hospital	Blood											Urine					Remarks
					Carbon Dioxid, Volume per Cent.	Urea N, Mg. per 100 C.c.	Incoagulable N, Mg. per 100 C.c.	Uric Acid, Mg. per 100 C.c.	Creatinin, Mg. per 100 C.c.	Cholesterol, per Cent.	Sugar, per Cent.	Hemoglobin, per Cent.	Erythrocytes	Leukocytes	Polymorphonuclears	Albumin	Sugar	Acetone	Diacetic	Microscopic Examination (Casts)	
1	5	M	19	1	40.4	22.4	62.5	3.0	3.0	.....	0.220	..	.....	.....	..	.....	.....	.....	.....	.....	Admitted moribund
2	7	M	3	2	41.4	25.2	50.3	1.5	2.8	.....	0.095	..	.....	.....	..	.....	.....	.....	.....	.....	Premature, no temperature, died
3	10	F	7	20	44.0	19.6	49.0	2.2	1.3	.....	0.112	78	5,500,000	9,400	64	Faint trace	Negative	Negative	Negative	Positive	Stools good before death
					62.4	15.4	30.8	3.0	1.2	0.100	0.095	86	5,100,000	.....	..	Faint trace	Negative	Positive	Positive		
4	10	M	4	4	53.2	24.2	....	...	...	.....	.....	84	.....	7,400	64	Negative	Negative	Positive	Positive	Negative	Terminal convulsion
5	8	F	10	1	42.4	....	49.0	2.5	2.2	.....	0.140	..	.....	.....	..	.....	.....	.....	.....	.....	Premature, died
6	12	F	2	9	43.8	16.8	76.0	2.2	2.2	.....	0.175	..	.....	15,000	34	Negative	Negative	Negative	Negative	Negative	Premature, home, well
					62.4	19.6	31.2	2.2	1.8	0.150	0.085	88	.....	24,000	42						
7	11	F	7	11	41.8	49.0	112.7	6.5	2.0	0.100	0.105	72	.....	11,000	82	Negative	Negative	Negative	Negative	Negative	Home, well
					39.0			1.2	2.5		0.115										
8	6	M	1	1	44.0	....	94.2	...	...	.....	0.180	92	.....	15,000	70	Very faint	Positive	Positive	Negative	Negative	Undernourished, died
9	4	F	2	1	42.0	82.6	119.6	9.0	6.6	.....	.....	..	.....	.....	..	Very faint	Positive	Positive	Positive	.....	Premature, no temperature, died
10	3½	M	18	3	39.2	36.4	81.9	5.0	1.9	.....	0.125	..	.....	.....	..	Very faint	Negative	Negative	Negative	Positive	Terminal convulsion
11	6	M	5	4	43.3	39.2	89.8	5.7	3.5	.....	0.113	87	4,000,000	.....	..	Very faint	Negative	Negative	Negative	Positive	Well developed child, terminal pneumonia
																Very faint	Positive	Negative	Negative	Positive	
12	8	F	7	29	44.3	50.4	95.5	4.6	2.8	0.100	0.120	..	4,700,000	9,400	58	Very faint	Negative	Negative	Negative	Positive	Died
					41.2	71.4	115.5	4.4	4.0	0.150	0.170										
					63.4	71.4	136.0	2.5	2.0		0.120						Negative	Negative	Negative	Positive	
13	6	F	6	8	20.0	26.8	63.3	3.0	1.5	.....	0.085	..	.....	12,000	62	Trace	Negative	Negative	Negative	Positive	Terminal convulsion (premature twin)
14	6½	F	21	17	31.9	11.2	30.9	1.9	1.4	0.160	0.130	71	.....	12,000	48	Faint trace	Negative	Negative	Negative	Negative	Undernourished, no temperature, well
15	22	M	4	3	44.3	16.8	32.3	1.5	1.4		0.092										
16	1½	F	2	3	34.7	21.0	47.8	1.4	1.2	.....	0.107	112	5,400,000	27,000	88	Trace	Negative	Negative	Negative	Positive	Died
					23.3	32.2	66.5	4.5	2.4	0.210	0.090	..	.....	.....	..	.....	.....	.....	.....	.....	Premature, subnormal temp., died
17	12	F	6	1	30.4	50.4	126.0	5.2	2.8	0.182	0.150	..	.....	.....	..	.....	.....	.....	.....	.....	Hospital 2 hours, died
18	7	F	7	1	28.6	....	97.0	...	...	.....	0.230	..	.....	.....	..	.....	.....	.....	.....	.....	Hospital 2 hours, died
19	5½	M	7	1	24.6	113.4	178.5	4.8	3.6	.....	0.132	..	.....	.....	..	.....	.....	.....	.....	.....	Hospital 1 hour, died
20	7	M	4	13	30.0	43.4	81.3	2.1	1.2	.....	0.264	71	3,500,000	.... .	..	Trace	Positive	Trace	Negative	Positive	Transfusion, died
21	5	M	14	1	29.5	11.2	44.4	2.5	1.8		0.133										
22	5	F	7	2	32.5	....	83.7	...	...	.....	0.070	..	.....	.....	..	Trace	Negative	Negative	Negative	Positive	Died
23	3½	M	5	6	27.4	43.4	92.1	5.7	3.5	.....	0.204	..	.....	.....	..	Trace	Negative	Negative	Negative	Positive	Died
					19.5	....	152.0	4.6	4.7	.....	0.080	..	6,400,000	18,000	44	Trace	Negative	Negative	Negative	Positive	Died
					38.5	84.0	147.3	12.5	4.8		0.060		4,800,000								

In order to ascertain whether there was any relationship between the clinical symptoms and the blood findings, examinations were made of the urea, nonprotein nitrogen, uric acid, creatinin, carbon dioxid, sugar and cholesterol.[7] In this way we have investigated twenty-three cases. Unfortunately, because of the grave condition of some of the cases, the length of time under observation and other circumstances, most of the cases had only one blood examination; yet in every case at the time the blood was taken, the children presented the typical symptoms of apathy, coma, vomiting and diarrhea.

Attempting an analysis, it would seem that we could divide our cases into four groups.

In the first group, the blood in regard to nitrogen partitions, cholesterol, sugar, carbon dioxid content was fairly normal. In one of these cases we did a second examination with the same result. These cases presented a clinical picture not differing from that of the others.

A second group of six cases (for convenience called uremic cases) had a normal carbon dioxid content, but the nitrogen constituents were markedly increased. This increase took in all the nitrogen substances which we examined. One of these patients was ill for over a period of weeks, and in this case we had the opportunity of making three examinations, all giving the same results. The urine in this group was not very different from that in the cases with normal blood findings, except that albumin and casts were more frequently found. That this high nitrogen retention was, perhaps, not due to diminished blood volume alone can be inferred from the fact that in some cases the hemoglobin estimations and red blood cell count were not excessively high.

In the third group, consisting of four cases, the only change from the normal was a diminished carbon dioxid content. The blood sugar and nitrogenous elements of the blood were normal. In one of these cases, a second blood examination was taken when the child was recovering. A normal carbon dioxid and other normal figures were obtained.

A fourth group of seven cases was a combination of the second and third groups—a nitrogen retention with a low carbon dioxid content. These cases presented no clinical difference from the others. In two of these cases we were able to make repeated examinations, one subsequently showing slightly less nitrogenous retention.

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7. Methods: Urea—urease (Marshall); nonprotein nitrogen—digestion and titration; uric acid and creatinin with Kuttner's modification of Folin's method; sugar—with Epstein's modification of Benedict's method; cholesterol—Bloor's method; carbon dioxid—Van Slyke's gasometric method.

Schloss also made a number of blood examinations in this type of case and found that the cases could be divided into much the same groups.

In the course of our examination for the uric acid content of the blood, it was noticed that after precipitating the uric acid with silver lactate mixture, the color obtained with the filtrate, using only the phosphotungstate, was exceptionally intense when compared with the filtrate from normal cases. This was noted in some of the cases in which there was no nitrogen retention. Whether this reaction is due to phenol [8] we are not prepared to say. Further investigation relative to the recent work of Tisdall [9] with the phosphotungstic-phosphomolybdic reagent and its bearing on phenols, is being pursued.

From the above it would appear that in some cases the blood chemistry is normal; in others there is a diminished carbon dioxid content; in still others only a retention of nitrogenous products and no acidosis, and finally, there is a group with both a nitrogenous retention in the blood and an acidosis. Most likely the underlying factor is the same in all groups.

Finkelstein [10] and his co-workers have ascribed this toxic symptom complex to the absorption of some of the food principles through a damaged or undamaged gut.

Escherich,[11] Libman,[12] Davidson [13] and many others have tried to ascribe some of these cases as being due to an invasion of a streptococcus or organisms of the dysentery group.

Recently Moro,[14] Bessau [15] and their co-workers have shown that there is an invasion of the duodenum by the *Bacillus coli* in these cases. They believe that these symptoms may be due to the action of these bacteria on the food or to the absorption of products of the bacteria themselves. Pursuing this idea further, Plantenga [16] in Holland and Hamburger [6] in Berlin, treated these patients with subcutaneous injections of a polyvalent *B. coli* horse serum with encouraging results.

In our treatment, the main object was to maintain the water balance, the etiology and the processes of this condition being as yet poorly understood. Glucose solution was used partly for nutrition and partly as a diuretic. Sodium bicarbonate solutions were not used, for it

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8. Folin, O., and Denis, W.: J. Biol. Chem. **12**:239, 1912.
9. Tisdall, F. F.: J. Biol. Chem. **44**:409, 1920.
10. Finkelstein, H.: Lehrb. d. Säuglingskrankh. 1911, Part 2, pp. 189-279.
11. Escherich, T.: Jahrb. f. Kinderh. **49**:137, 1899.
12. Libman, E.: Centralbl. f. Bakteriol., Parasitenk. u. Infektionk. **22**:376, 1897.
13. Davison, W. C.: Bull. Johns Hopkins Hosp. **31**:225, 1920.
14. Moro, E.: Jahrb. f. Kinderh. **84**:1, 1916.
15. Bessau, G., and Bossert, O.: Jahrb. f. Kinderh. **89**:213, 269, 1919.
16. Plantenga, B. P. B.: Jahrb. f. Kinderh. **86**:175, 1917.

seemed useless to try to combat the carbon dioxid content only temporarily, and, secondly, the carbon dioxid content was frequently normal.

The food was breast milk or protein milk. In most cases no food seemed to be tolerated in any amount. In one case, a malt soup mixture seemed to do no harm. The fluid of the body was mostly maintained by means of subcutaneous and intraperitoneal injections. Transfusion was only done once so that we cannot report on its value.[17]

CONCLUSIONS

1. These cases seem to occur almost wholly in the summer months and are very rare in entirely breast fed children.

2. These cases are always accompanied by vomiting and diarrhea.

3. The etiologic factor or factors are as yet unexplained.

4. The carbon dioxid content and the nitrogenous constituents of the blood may be normal. Some of these cases may show only diminished carbon dioxid content. Others show a normal carbon dioxid content, but a markedly increased retention of the nitrogenous constituents, and, finally, some cases show both a diminished carbon dioxid content and a nitrogenous retention. Therefore, our studies would indicate that acidosis based on a lowered carbon dioxid content of the blood is not a constant or uniform finding.

The sugar and cholesterol content of the blood may be normal or high. There is apparently no relation between these constituents and either the nitrogenous or the carbon dioxid content.

5. In spite of all the variations in the chemical composition of the blood, there is no difference in the clinical picture or in the history of these cases.

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17. Since the completion of this paper there has appeared *(Am. J. Dis. Child.* **20**:461 [Dec.] 1920) a very comprehensive paper by Marriott which deals, in part, with acute toxic nutritional disorders. His conclusions are that the toxic symptoms can be ascribed to a water loss from the body and a resulting concentration of the blood. This increased concentration of the blood in acute toxic conditions similar to the above has been confirmed by Rominger *(Ztschr. f. Kinderh.* **26**:23, 1920) who also shows that this concentration persists for a long time during the reparative stage.

DIPHTHERIA AMONG IMMUNIZED CHILDREN *

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My object in reporting these cases is to have on record the fact that diphtheria can occur among children who possess either natural immunity or who have been immunized by the toxin-antitoxin procedure. If we are to utilize our knowledge of diphtheria immunity intelligently, without prejudice to the community or to the child who has suspicious sore throat, and raise the bars of precautions against a disease of so many possibilities, we must be sure that our interpretative value of a negative Schick reaction will stand the test of time and experience, and particularly that immunity, as obtained by the toxin-antitoxin instillation, is sufficiently universal in its application that not even an occasional exception will alter its value. An immunity recorded by a negative Schick reaction should not be sufficient, and only when a sufficient number of Schick negative immunized children have been exposed to diphtheria contagion and have escaped the disease can a proper value be placed on it. An experience which I and my co-workers have had in a carefully supervised orphan asylum,[1] has taught us that diphtheria in epidemic form can occur among immunized children, at least to say now that the value of a negative Schick reaction is not universal, and as a result further studies and clinical observations must be made before its exact value can be computed.

I am aware that these cases of diphtheria among immunized children are probably the first on record, at least where virulency test was taken, and, therefore, exception may be taken that our experience can be due to either faulty technic, imperfect toxin or antitoxin, or we are even dealing with an epidemic of septic sore throat in diphtheria carriers. All these possibilities have been considered and excluded and with the clinical picture and behavior of the cases there can be no other conclusion but that they were true cases of clinical diphtheria.

The children at the orphan asylum had all been given the Schick test, and our figures correspond so closely with the results of other investigators (40 per cent. positive and 60 per cent. negative) that no fault should be found with either technic or our material. The Schick positive children were all immunized by three doses of toxin-antitoxin,

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* Read before the New York Physicians' Association, Oct. 28, 1920.

1. Israel Orphan Asylum.

injected at intervals of one week, and after three months they were retested for immunity. A small group, however, still persisted with either a faintly positive or a strongly positive Schick reaction. The weakly positive cases were again tested after a lapse of several weeks, and the few that still reacted, together with the strong positive cases, were given an additional dose of toxin-antitoxin, the latter group receiving, however, a somewhat stronger dose than the three previous doses.

TABLE 1.—FINDINGS WITH SCHICK TEST IN SIXTY CASES

	Reaction	Number	Per Cent.
First test	Negative	36	60
Second test	Positive	24	40

Table 2 shows that two of the positive cases became negative fifteen months aften the T-A injections.

TABLE 2.—TIME OF TOXIN-ANTITOXIN INJECTION AND SCHICK CONTROL OF THE TWENTY-FOUR POSITIVE CASES

	Date	22 Cases	2 Cases
Schick I	3/25/19	Positive	Positive
T-A I	4/18/19	.....	.....
T-A II	4/25/19	.....	.....
T-A III	5/ 2/19	.....	.....
Schick II	8/ 1/19	Negative	Positive
Schick III	12/20/19	Negative	Positive
Schick IV	4/21/20	Negative	Positive
Schick V	8/19/20	Negative	Negative

In this manner all our children were finally made Schick negative with the exception of two, who remained persistently positive even after additional tests. It is interesting to note, however, that in the last Schick test made on all the children, August, 1920, these two positive cases, after a lapse of fifteen months from the time the three toxin-antitoxin immunizing injections were given, finally became Schick negative. The question naturally arises whether the toxin-antitoxin had any influence on this end result or whether it was due to the general tendency of natural immunity which the human organism acquires as it grows older. My own impression is that the toxin-antitoxin had no part in the Schick test results, for experience has shown that the toxin-antitoxin shows its influence usually within from three to four months after its injection.

It is our practice to make throat cultures of all new admissions to the observation ward where they remain at least three weeks, depending, of course, on whether any contagion has appeared among them, and when finally admitted to the dormitories as permanent inmates, we are certain they are diphtheria-carrier free. As a further precaution, all

permanent inmates are cultured at least once a year, sometimes oftener, depending on conditions, and as a result of this precaution, we feel that we are at all times free from diphtheria carriers.

Our food supply is regulated and under constant supervision to make sure that no contamination occurs; our milk supply, particularly, is thoroughly supervised and comes from a reputable dealer of this city. The children throughout the institution receive the same food and no outside food, particularly from friends and relatives who are allowed to visit but several times a year, is permitted, so that an infection, such as diphtheria or streptococcus sore throat, occurring from this source would be more or less evenly distributed throughout the institution and not confined to one dormitory as has occurred with this outbreak of diphtheria.

This outbreak of diphtheria was limited to one dormitory consisting of twenty-nine children. In all we had eight cases, beginning with three cases and spreading at intervals of from one to several days until eight children were ill (Table 3). Clinically, the appearance of the membrane, its location on tonsil and pharynx, moderate temperature, absence of toxic symptoms, which are usually present in a tonsillitis or a septic sore throat, gave the impression of a diphtheria throat, but as we had no suspicion that diphtheria can be possible in immunized children, antitoxin was not injected till the report as to the cultures was returned. When it became evident that we were probably dealing with diphtheria infection, we injected these three children, but waited with the prophylactic injections on the other children till we could test for the virulency [2] of these positive cultures.

In the meantime, before the report of the virulency test was returned, the infection continued to spread at intervals of from twenty-four to forty-eight hours until we had a total of eight cases. Clinically, these additional cases showed diphtheritic throat, positive cultures and when the virulency test later returned positive we were sure that we were dealing with a positive Klebs-Loeffler infection. It is also interesting to note (Table 3, Schick III, 12/20/19, in Table 2) that given the Schick test and which showed results similar to those obtained on previous tests, thereby eliminating the possibility of some Schick negative reactions having turned to Schick positive. It is also interesting to note that four children possessed a natural immunity, and three children had an acquired immunity as the result of the antitoxin injection and one child was positive up to the time the infection occurred.

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2. Cultures and virulence tests were made by the New York City Board of Health. Not only taken by department but under special supervision of head of department.

TABLE 3.—Clinical Record of Diphtheria Cases

Case	Name	Age	Date of Onset	Class	Membrane; Location and Character	First Temperature	Temperature 12 Hours after Antitoxin	Temperature 24 Hours after Antitoxin	Cultures			Virulence
									I	II	III	
1	M. S.	3 yrs. 8 mos.	12/23	A	Thin, grayish, involving both tonsils and the pharynx	102.8	101.2	100.6	Positive 12/24/19	Negative 1/15/20	Negative 1/20/20	12/31/20 Positive
2	R. P.	4 yrs. 8 mos.	12/23	B	Pharynx and left tonsil; grayish, thick, unbroken	103.0	102.4	101.0	Positive 12/24/19	Negative 1/15/20	Negative 1/20/20	Positive
3	M. M.	5 yrs. 5 mos.	12/23	B	Right tonsil and pharynx; in patches	103.0	102.6	102.0	Positive 12/24/19	Negative 1/15/20	Negative 1/20/20	Positive
4	A. G.	3 yrs. 6 mos.	12/26	A	Both tonsils; pultaceous, dirty gray	104.0	102.0	101.8	Positive 12/28/19	Negative 1/15/20	Negative 1/20/20	Positive
5	L. S.	3 yrs. 9 mos.	12/28	C	Right tonsil; in patches	102.2	100.0	99.0	Positive 12/30/19	Negative 1/15/20	Negative 1/20/20	Positive
6	M. S.	5 yrs. 2 mos.	12/29	B	Both tonsils; pultaceous	102.2	101.0	100.0	Positive 12/30/19	Positive 1/15/20	Negative 1/20/20	Positive
7	H. S.	2 yrs.	12/30	A	Unbroken grayish; spreading over both tonsils and across pharynx	102.4	104.8	103.4	Positive 12/31/19	Negative 1/15/20	Negative 1/20/20	Positive
8	B. S.	2 yrs. 8 mos.	12/31	A	In patches; involving both tonsils and pharynx	103.0	103.0	102.0	Positive 12/31/19	Negative 1/15/20	Negative 1/20/20	Positive

A = Children naturally immune.
B = Children immunized by T. A.
C = Children with persistent positive Schick reaction.

The main possibility to exclude in this epidemic is that these were cases of streptococcus sore throat in diphtheria carriers. It is difficult to understand, however, how we can include streptococcus sore throat, when we consider that all these cases occurred in one dormitory, with the supply of food the same throughout the institution. Furthermore, these children did not behave as children do who have a septic sore throat, neither was the appearance or location of the membrane, which was present in several cases on the pharynx as well, the same, nor was the intensity of the subjective symptom the same; and, what is most important, they all showed a virulent Klebs-Loeffler bacillus which disappeared a reasonable time after injection of antitoxin. We have here, then, I am sure, all clinical and laboratory evidence of a positive diphtheria infection.

CONCLUSIONS

In conclusion, permit me to reiterate that these eight cases are strong evidence that immunization is not absolutely proof against clinical diphtheria, and that we were dealing with a true Klebs-Loeffler infection for the following reasons: (1) character of the membrane, —dull gray, no surrounding hyperemia; (2) absence of prostration, —children were playful, while in septic sore throat infection the prostration is intense, out of all proportion to local involvement; (3) the disease was limited to one dormitory. In septic sore throat, food borne disease usually would have been more evenly distributed throughout the building; (4) occurrence of cases—gradually, from day to day. In septic sore throat, the onset would have been more or less simultaneous. (5) Positive virulent cultures were obtained in all cases which turned negative approximately two weeks after antitoxin injection; (6) absence of positive cases in other dormitories; (1) if these were merely persistent diphtheria carriers with no clinical reaction, it is fair to assume that some should remain so even after injection of antitoxin; (8) immediate improvement of cases on receiving antitoxin; (9) immediate cessation of spread of the disease on administration of prophylactic doses of antitoxin to exposed children in the same dormitory. (10) Is it possible that streptococcus sore throat would have attacked only carriers and avoided the noncarriers?

I am indebted to Drs. Appel, Popper and Bloom for their kind cooperation and assistance in this work.

EOSINOPHILIA OCCURRING IN CHOREA*

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There are few subjects about which so much has been written and said, and yet so little is understood as about chorea. Until the etiology of this disease, or symptom, as the case may be, is determined, we can hope for little headway. It is with a desire to add a bit of evidence along such lines that I present this preliminary report of work I am undertaking.

Kowalewsky was probably the first to suggest syphilis as the etiology of chorea. Milian [1] then presented two cases with positive Wassermann reactions, and by 1914 he became established in the opinion that all chorea is syphilitic in origin.[2] Comby [3] challenged this theory, contending that a positive Wassermann reaction is no better evidence in favor of syphilis as the cause of chorea, than a positive tuberculin reaction is that tuberculosis is the cause. Guillian pointed out that the pathology in chorea is not that of syphilis of the nervous system, nor do they act the same clinically.

Foti [4] in seventeen cases reported only one case as being free from syphilitic taint. In only thirteen cases, however, was syphilis unmistakable. He considers syphilis as being the principal predisposing factor in chorea, causing instability of the nervous system to such a degree that diverse causes, such as infections, emotional stress, or metabolic disturbance may bring on chorea. Babonneix [5] and Grabois,[6] reviewing 145 and 136 cases of chorea, respectively, from the service of Hutinel, found slight or at least insufficient evidence that syphilis was the origin. Koplik,[7] in 1914, examined ten cases, eight of which gave a negative Wassermann reaction. In the remaining two cases the results were unsatisfactory, though not positive.

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* Received for publication, Dec. 22, 1920.
* From Children's Mercy Hospital.
* Read before Central States Pediatric Society, St. Louis, Oct. 13, 1920.

1. Milian: Bull. et mém. Soc. méd. d. hôp. de Par. **33**:955, 1912; ibid. **34**: 628, 1912.
2. Milian: Bull. et mém. Soc. méd. d. hôp. de Par. **37**:368, 1914.
3. Comby: Bull. et mém. Soc. méd. d. hôp. de Par. **39**:238, 1915.
4. Foti, P.: Pediatria **27**:579 (Sept.) 1919; abstr., Arch. Pediat. **37**:461 (Aug.) 1920.
5. Babonneix: Bull. et mém. Soc. méd. d. hôp. de Par., Series 3 **34**:671, 1912.
6. Grabois: Thése de Paris, 1913, No. 298.
7. Koplik: Arch. Pediat. **32**:561, 1915.

The great mass of evidence is against syphilis as a constant factor in chorea.

Some good results in the treatment of chorea with arsphenamin, even in cases proven nonsyphilitic, have been reported by Bokay, Haines, Hohn and Salinger,[8] Szametz,[9] Marie and Chatelin.[10] Flatau reported unfavorably on this method of treatment. Koplik reported the treatment of nine cases with arsphenamin. In seven he could see no effect. Of the remaining two cases, one developed nephritis and one had a relapse.

The seeming close relationship of rheumatism, endocarditis, and chorea, and accepting as we must the bacterial origin of endocarditis at least, and the frequency with which focal infections are found to exist with these diseases, draws one's attention toward bacterial infection as a causative factor in chorea also.

Westphall, Wassermann and Malkoff [12] and Poynton and Payne [13] reported isolating a diplococcus from the spinal fluid, with which they were able to produce endocarditis, pericarditis, arthritis, or twitching in animals by intravenous inoculation. Donath [14] reported *Staphylococcus pyogenes aureus* and *S. Albus* isolated from the spinal fluid during life in a case of chorea. Collins [15] reported a case cured by an autogenous vaccine made from a coccus in the spinal fluid. Passini [16] was unable to get any growth from the spinal fluid in five cases.

We have had reports of bacilli, staphylococci, diplococci, streptococci, diplococci in chains, and diphtheroids being isolated from the blood of chorea patients. Moderate agglutination of some of these organisms by the blood from chorea patients has been claimed by Camisa.[17] Collins [15] found a diplococcus, and Richards [18] and La Fetra [19] report two cases each of *Streptococcus viridans*. Koplik was unable to isolate any organism after many attempts.

In 1918 Quigley [20] wrote on the bacteriology of chorea, and Cronk [21] on the relation between rheumatism and chorea. Morse and Floyd,[22]

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8. Salinger: München. med. Wchnschr. **58**:25, 1912.
9. Szametz: München. med. Wchnschr. **59**:2333, 1912.
10. Marie and Chatelin: Bull. de l'Acad. de méd. Par., Series 3 **68**:507, 1912.
11. Flatau: München. med. Wchnschr. **59**:2102, 1912.
12. Wastphall, Wassermann and Malkoff: Berl. klin. Wchnschr. **36**:638, 1899.
13. Poynton and Payne: Lancet **2**:1760, 1905.
14. Donath: Ztschr. f. d. ges. Neurol. u. Psychiat. **4**:91, 1910.
15. Collins: Brit. M. J. **1**:220, 1913.
16. Passini: Wien. klin. Wchnschr. **27**:1363, 1914.
17. Camisa: Centralbl. f. Bacteriol. **57**:99, 1910.
18. Richards: J. A. M. A. **62**:110 (Jan. 10) 1914.
19. LaFetra: Arch. Pediat. **32**:135, 1915.
20. Quigley, W. J.: J. Infect. Dis. **22**:198 (March) 1918.
21. Cronk: Lancet **2**:646 (Oct. 11) 1919.
22. Morse and Floyd: Am. J. Dis. Child. **12**:61 (July) 1916.

in 1916, reviewed the literature to that date quite thoroughly, and reported their own studies on blood and spinal fluid cultures, with some animal inoculations, in a series of twenty-six cases of chorea. They reached the following conclusions: "Our investigations show that syphilis plays no direct part in the etiology of chorea. Our results suggest that a micro-organism or group of micro-organisms may be the cause of chorea. They seem to show that if chorea is caused by a micro-organism, the source of infection is ordinarily in the tonsils or teeth. They tend to confirm the belief that there is an intimate relation between chorea, rheumatism and endocarditis."

In 1916, Goodman [23] reported some favorable results from autoserum therapy. Since that time Moffett,[24] Faber [25] and Brown, Smith and Philips [26] have reported their results with his method of treatment.

Porter [27] used horse serum in place of autoserum intrathecally with some good results. Haneborg,[28] in 1916, gave a report on the treatment of chorea with thymus gland, suggesting the possibilty of a disordered thymus function playing a rôle in the etiology of chorea.

The literature yields surprisingly little on the study of the blood in chorea. No other disease that occurs with the frequency of chorea, and with such distressing symptoms, has had so little attention paid to the blood. Cabot [29] says: "Chorea showed in twelve cases normal blood, except for increased percentages of eosinophils, as in Zappert's two cases which Louga confirms." Brown,[30] making twelve observations on two cases of chorea noted an eosinophilia varying from 5.2 to 9.5 per cent.

Macalister [31] found in his first two cases examined, 20 and 16 per cent. eosinophils, respectively, and in later cases found an eosinophilia in all but one case. The stools were free from ova, and no other explanation could be found for the eosinophilia. Eosinophilia was not present in cases of rheumatism examined by him. Leopold [32] reported twenty cases of chorea, with eosinophilia varying from 1 to 16 per cent. He claims a higher eosinophilia in a second attack of chorea than in a first attack. He found eosinophilia present in a high proportion of cases examined, and could offer no explanation for this except chorea, other causes being sought as far as possible.

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23. Goodman: Arch. Pediat. **33**:649 (Sept.) 1916.
24. Moffett: Med. Rec. **92**:414 (Sept. 8) 1917.
25. Faber: Calif. State J. M. **15**:27 (Jan.) 1917.
26. Brown, Smith and Philips: Canad. M. A. J. **9**:52 (Jan.) 1919.
27. Porter, L.: Am. J. Dis. Child. **16**:109 (Aug.) 1918.
28. Haneborg: Norsk Mag. f. Lægevidensk. **77**:1040 (Aug.) 1916.
29. Cabot, R. C.: Clinical Examination of the Blood, Ed. 3, New York, William Wood & Co., p. 313.
30. Brown, T. R.: Maryland M. J., 1902.
31. Macalister, C. J.: Brit. M. J. **2**:514, 1909.
32. Leopold, S. S.: New York M. J. **100**:225, 1914.

Results of Studies of Eosinophilia in Children

Name	Percentage Eosinophils							Days Elapsing Between Counts							High Percentage	Low Percentage	Average Percentage	
Lena S.	7							..	..	..	..	..	..	..	7	7	7.0	
Mary S. P.	23	19	7	13	..	..	..	0	2	7	14	..	..	..	23	7	15.5	Had attack one year ago; tonsils badly infected
Mable G.	14	..	..	..	..	..	..	..	..	..	..	..	..	..	14	14	14.0	Goiter; no ova in stools
Ettie C.	1	6	3	9	..	..	..	0	2	4	7	..	..	..	9	1	4.75	Very mild case
Rose R.	4	6	7	3	..	..	..	0	6	2	14	..	..	..	7	3	5.0	First attack; tonsils removed in six weeks
Rose. R.	1	5	3	3	..	..	..	0	2	7	10	..	..	..	5	1	3.0	Second attack 11 months later; no rheumatism or endocarditis
Ernest A.	16	14	17	6	..	..	..	0	7	4	10	..	..	..	17	6	13.25	No ova in stools; marked obesity
Christine P.	7	1.5	3	2	3	..	..	0	9	14	7	5	..	..	7	1.5	3.3	Very severe type chorea major
Mary V.	2	9	3	..	..	..	..	0	9	7	..	..	..	..	9	2	4.66	
Lloyd R.	3	5	1.5	..	..	..	..	0	9	7	..	..	..	..	5	1.5	3.17	
Violet M.	0	9	..	..	..	..	..	0	7	..	..	..	..	..	9	0	4.5	Clinical syphilis; Wassermann 4 plus
Ernestine M.	3	13	..	..	..	..	..	0	7	..	..	..	..	..	13	3	8.0	
Violet W.	9	0	1.5	..	..	..	..	0	9	10	..	..	..	..	9	1.5	3.5	
A. B. S.	5	1	3	2	..	..	..	0	19	7	7	..	..	..	5	1	2.75	
Mary S.	11	7	..	..	..	..	..	0	7	..	..	..	..	..	11	7	9.0	Had sister in hospital with chorea major several months ago
Margaret W.	3.5	2	7	9	5	..	..	0	3	9	14	7	..	..	9	2	5.3	First attack, another in 8 months
Margaret W.	11	..	..	..	..	..	..	..	..	..	..	..	..	..	11	11	11.0	This is second attack, 8 months after first
Helen T.	16	9	6	7	5	2	..	0	8	7	8	10	11	..	16	2	7.5	Stools not examined
Ethel C.	3.25	4	3	..	..	..	..	0	5	7	..	..	..	..	4	3	3.41	
Jessie S.	2	..	..	..	..	..	..	..	..	..	..	..	..	..	2	2	2.0	
David S.	19	..	..	..	..	..	..	..	..	..	..	..	..	..	19	19	19.0	No ova in stools
Valencia P.	13	..	..	..	..	..	..	..	..	..	..	..	..	..	13	13	13.0	No ova in stools
Kenneth V. H.	9	14	12	7	..	..	..	0	7	4	4	..	..	..	14	7	10.5	No ova in stools}Brothers
Keith V. H.	3	3	3	1	4.5	2	..	0	7	4	4	10	?	..	4.5	1	2.70	No ova in stools}same date
Henry E.	5	..	..	..	..	..	..	..	..	..	..	..	..	..	5	5	5.0	
Dolly D.	4	6	6	..	..	..	..	0	4	3	..	..	..	..	6	4	5.33	
Thelma A.	7	14	7	9.5	13	2	6	0	14	9	3	9	10	19	14	2	8.36	
Jos. M.	5	3	2	4	..	..	..	0	9	14	9	..	..	..	5	2	3.5	
Edith C.	4	3	3	6	..	..	..	0	9	3	9	..	..	..	6	3	4.0	
Anna S.	22	12	13	8	..	..	..	0	4	4	2	..	..	..	22	8	13.75	First attack; no ova in stool
Anna S.	23	22	26	18	22	..	..	0	7	7	10	9	..	..	26	18	22.2	Second attack 10 months later; no ova in stool
Helen W.	12	3	3	2	5	..	..	0	17	16	5	9	..	..	12	2	5.0	Recovery very slow; stool negative
Mary G.	17	13	17.5	11	9.5	..	..	0	9	3	9	14	..	..	17.5	11	13.6	Stool negative
Elizabeth H.	2.5	2	3	4	..	..	..	0	9	13	14	..	..	..	4	2	2.88	Last two counts made in O. P. D.
Dominic P.	18	14	..	..	..	..	..	0	5	..	..	..	..	..	18	14	16.0	No examination of stool
Margaret G.	18	8	..	..	..	..	..	0	10	..	..	..	..	..	18	8	13.0	No ova in stool
Gertrude M.	7	4.5	4	4	..	..	..	0	5	7	8	..	..	..	7	4	4.88	The following year developed rheumatism and endocarditis
John H.	7	..	..	..	..	..	..	..	..	..	..	..	..	..	7	7	7.0	
Le Verne S.	1	..	..	..	..	..	..	..	..	..	..	..	..	..	1	1	1.0	
Juanita I.	7	12	..	..	..	..	..	0	7	..	..	..	..	..	12	7	9.5	
Dorothy B.	3	6	7	5	5	..	..	0	3	16	4	5	..	..	7	3	5.2	
Wilma K.	6	5	7	5	5	..	..	0	3	16	4	5	..	..	7	5	5.6	
Hazel Van C.	8	6	5	3	..	..	..	0	7	10	4	..	..	..	8	3	5.5	
Average															10.35	5.24		
General average all counts	7.60																	

In my series of cases I have paid attention principally to the blood, and in the blood particularly to the percentage of eosinophilia present. It was begun in 1916 and continued to date, except for a period of a few months when I was unfortunately obliged to abandon the work.

In a few cases only a single count was obtained, these cases not being easily available for more counts. It was impossible accurately to determine the period in the disease when each count was taken, as the accuracy of the history as to onset depended entirely on how keen the parents were in observation, and most of these cases were seen on my hospital service, or in the outpatient department clinic. There was no connection between the severity of the symptoms, and the percentage of eosinophils found, a comparatively mild case sometimes giving a much higher count than a very severe case, and in some of my most severe cases, in which restraint was required, a low percentage of eosinophils was noted. Nor did the counts vary regularly before, during, or after some temporary exacerbation of the symptoms. No case was included in which the diagnosis was not perfectly clear. In no case reported here were there any parasites or lesions on the skin or scalp to account for an eosinophilia. A careful examination for intestinal parasites was made on most of these children, in all but one case in which a particularly high count was found. This was omitted in a few cases.

None gave a history of asthma or eczema. A Wassermann examination was made on most of these children. The proportion of positive reactions ran slightly less in this group than in the whole group of patients in this hospital tested, though some were frankly syphilitic clinically as well as having a positive Wassermann reaction. Focal infection in tonsils, and especially teeth, was, of course, common in this class of patients, but not any more so than in the average of patients at this clinic. Rheumatism and endocarditis were peculiarly rare in the histories of these children. The ages ranged from 7 to 14 years.

There were twenty-nine girls and eleven boys. Three girls were seen during both the first and the second attacks, the second attack coming on in the year following the first attack. One girl had a marked goiter. Two boys were brothers and were brought into the hospital at the same time, with chorea of about equal severity. In some cases treatment was begun before the first blood examination, in others not. The type of treatment was not the same in all cases. No autoserum treatment was given.

The blood films were prepared with ordinary glass slides by allowing a drop of blood to follow the edge of one slide along the surface of the other. This gave an uneven streaked end to the film, and this

was always included in the examination of the slide. I found that the eosinophils were in higher percentage in this portion of the preparation than in the main body of the film, a fact that I am at a loss to explain. The stain used was Wright's blood stain—secured from two different sources. To insure greater accuracy each count was of 900 white blood cells, the percentage of eosinophils being calculated from this count.

I have arranged my results in the accompanying table so that it may be seen at a glance just what was fonud.

The table presents my findings so clearly that there seems to be little need for further elucidation. The highest count was 26 per cent., the lowest 0, with a general average of 7.6 per cent. The criticism may be offered that in eight cases, and in a case during a second attack, only a single count was made, and that these counts should not be included in my averages. However, it seemed to me better to do so. Every possible effort to explain the eosinophilia in some way, other than chorea, was made.

I have been unable to make up my mind definitely as to the highest percentage of eosinophils that may be considered normal at a given age, knowing that in children we must allow for higher percentages than in adults. Within the age range here given, you may form your own conclusions in this respect. While some of these cases will easily fall within normal limits, others are far above. Certainly, the general average of 7.6 per cent. must be considered an increase of eosinophils, and I have considered all except five cases showing an eosinophilia some time during the series of counts.

The rise and fall in these counts could not in any way be connected with the clinical progress of the case, and I am at a loss to explain this feature.

What bearing this eosinophilia may have on the etiology of chorea, we are as yet in no position to discuss fully. That chorea is not often, if ever, syphilitic in origin, I believe is generally conceded. If chorea is due to a bacterial infection, whether specific or otherwise, is the eosinophilia due to the sensitization of the child to the invading organisms? Such a theory might be suggested by the work of Floyd and Baker.[33] This is hardly tenable, however, since we do not find this present in rheumatism according to Macalister,[31] nor do we find such an eosinophilia present in other types of general infection.

Is it possibly due to a toxemia as in the case reported by Deglos,[34] where eosinophilia was produced in an anemic patient, with enteritis,

33. Floyd and Baker: Boston M. & S. J. **175**:199, 1916.

34. Deglos, E.: Lyon méd. **128**:231 (May) 1919; abstr., J. A. M. A. **73**: 231 (July 19) 1919.

through periodic poisoning by carbon monoxid gas from a charcoal stove?

If it is a toxemia, may it not be due to an altered metabolism, resulting possibly from a hyperactivity of one of the glands of internal secretion, or a suppressed inhibition due to deranged or deficient function of such a gland, as Haneborg [28] suggests?

The known effect of the reproductive organs, particularly in the female, on the internal secretions, and the fact that chorea is not an uncommon complication of pregnancy, while not offering an argument, may have some significance in this connection.

To me it seems more probable that if chorea is the result of a general bacteremia, it acts on some body structure, possibly one or more of the endocrine glands, through a toxin or otherwise, than that the infection is a cerebral irritant per se. Such a course of action might also account for the eosinophilia present, through sensitization to a toxin, or to the superabundance of some secretion which is normal and hence gives no reaction in smaller quantities. It does not seem that a straight infection could do so.

Another explanation might be attempted, showing that the abnormal physiology of the nervous system itself reacts on other structures in some way, producing a substance which stimulates eosinophil production.

It is my hope that this preliminary report will stimulate further work on the etiology of chorea.

THE PRESENCE OF SUGAR IN THE URINE OF NEW BORN INFANTS BEFORE THE INTAKE OF FOODS *

FRANCES MILLIKIN

CHICAGO

Czerny and Keller [1] mention that Mesnil found sugar occasionally in the urine of infants during the first few days of life, and Nothman [2] found sugar in the urine of premature infants. The presence of sugar was shown by reduction tests, and in the case of Nothman the osazone was prepared which indicated the presence of lactose. By using the Benedict-Osterberg [3] method, Greenthal [4] showed that the urine of all infants contains sugar. This would be expected from the results obtained by Benedict, Osterberg and Neuwirth.[5] These authors found determinable quantities of sugar at all times, both in the urine of normal dogs, and those fasting for four-day periods, and in the urine of adults.

Thanks to the kindness of Dr. Sauer, we were able to obtain the urine of a series of new born infants for sugar determination.

The urine was collected during the period preceding the first feeding. None of the births was difficult, so that the results cannot be vitiated by the transitory traumatic glycosuria described by Hoeniger.[6] The method employed for the determination was that described by Benedict and Osterberg,[3] which has the important advantage of eliminating the possibility of the interference, in the determinations, of albumin, which occurs in the urine of the newly born. In all instances, duplicate determinations were made, all of which agreed very closely. In every case the urine was strongly acid to litmus. The first five cases are not recorded in the tables. They showed 0.036, 0.034, 0.072, 0.05 and 0.136 per cent. sugar, respectively.

Table 1 shows the quantitative determinations of sugar in the urine of individual infants. In Table 2, combined specimens from two or three infants, as indicated, were used. The amounts of urine per individual varied between 6 and 34 c.c. The amonts of total urinary

* Received for publication, Feb. 5, 1921.

* From the Otho S. A. Sprague Memorial Institute of the Children's Memorial Hospital.

1. Czerny and Keller: Des Kindes Ernährung, etc.
2. Monatschr. f. Kinderh. **8**:377, 1909.
3. Benedict and Osterberg: J. Biol. Chem. **34**: 195 (April) 1915.
4. Greenthal: Am. J. Dis. Child. **20**:556 (Dec.) 1920.
5. Benedict, Osterberg and Neuwirth: J. Biol. Chem. **34**: 217 (April) 1915.
6. Hoeniger: Deutsch. med. Wchnschr., **1**: 500 1911.

sugar for the collection period ranged from 1.722 to 27.948 mg., with an average of 9.536 mg. The concentration of sugar in Tables 1 and 2 varied between 0.027 and 0.166 per cent., with an average of 0.078 per cent. Too much importance should not be attached to averages for so few cases.

Benedict, Osterberg and Neuwirth [5] found sugar in the urine of adults collected for two hour periods in the morning before food was taken, in concentrations of from 0.04 to 0.16 per cent. for one subject and from 0.03 to 0.049 per cent. for another. Greenthal [4] showed sugar to be present in the urine collected for eight hour periods from infants on ordinary diets in concentrations of from 0.045 to 0.092 per cent. The twenty-four hour urine of a normal adult on ordinary diet contained from 0.042 to 0.22 per cent sugar, that of another from 0.04 to 0.126 per cent.

TABLE 1.—QUANTITATIVE DETERMINATION OF SUGAR IN URINE OF INFANTS

No.	Name	Amount	Sp. Gr.	Total Sugar	
				Per Cent.	Mg.
1.	Dixon	7 c.c.	1.011	0.078	5.467
2.	Keck	6 c.c.	1.007	0.028	1.722
3.	White	17 c.c.	1.006	0.027	4.607
4.	Brewster	34 c.c.	1.003	0.082	27.948
5.	Koran	9 c.c.	1.010	0.061	5.540
6.	Brown	9 c.c.	1.012	0.043	3.906
7.	Trueblood	10 c.c.	1.012	0.051	5.100
8.	Nein	15 c.c.	.....	0.140	21.420
9.	Foster	15 c.c.	1.016	0.100	15.000
10.	Perry	17 c.c.	1.010	0.072	13.308
11.	Farnsworth	11 c.c.	1.010	0.128	14.102
	Average	13.6 c.c.	1.009	0.073	10.738

In Table 3 two determinations of the unfermentable sugar are given. There is sufficient reason to accept the fermentable sugar as glucose, but the nature of the unfermentable sugar is not known. In this table the unfermentable sugar was present in lower percentages (12.6 and 30.8 per cent.) than in the urine of infants and adults on regular diets or in the urine of adults during the fasting period of the day. For example, in urine collected from adults during the two-hour period in the morning before food was taken, Benedict, Osterberg and Neuwirth found unfermentable sugar to constitute from 57 to 73 per cent. (at one time falling as low as 36.3 per cent.) of the total urinary sugar for one subject and from 41.8 to 71.0 per cent. for the other. For adults on mixed diets they found the twenty-four hour urine

specimens to contain unfermentable sugar constituting from 40 to 65 per cent. of the total urinary sugar. Greenthal [4] demonstrated that of the total urinary sugar of infants on ordinary diet, from 38 to 49 per cent. was unfermentable sugar.

TABLE 2.—Quantitative Determination of Sugar in Combined Specimens of Urine

No. Name	Amount	Sp. Gr.	Total Sugar	
			Per Cent.	Mg.
12. Horne ..... 13. Wells	23 c.c.	1.009	0.073	16.88
14. Pratt ..... 15. Bang ..... 16. Jones	25 c.c.	1.011	0.082	20.55
17. Friedlander .... 18. Benedict	21 c.c.	1.014	0.080	16.926
19. Blair ..... 20. Woodburn	30 c.c.	1.015	0.050	17.4
21. Morgan ..... 22. Morganson	12 c.c.	1.016	0.166	19.92
Average	11 c.c.	1.013	0.090	8.334
Average of Tables 1 and 2....	12.3 c.c.	1.011	0.078	9.536

The results of this series of urinary sugar determinations show that sugar does constantly occur in the urine of newly born infants before food is taken, and that it is present in about the same concentrations as in the urine of normal adults before food is taken in the morning.

TABLE 3.—Determinations of Unfermentable Sugar

No. Name	Total Sugar		Fermented Sugar		Unfermentable Sugar		Total Sugar
	Per Cent.	Mg.	Per Cent.	Mg.	Per Cent.	Mg.	Per Cent.
4. Brewster	0.082	27.948	0.0718	24.416	0.0103	3.532	12.6
12. Horne ..... 13. Wells	0.073	16.88	0.051	11.69	0.021	5.191	30.8

The range of concentrations can easily explain why sugar is sometimes found in the urine of the newly born by the usual copper reduction tests. For instance, Miss Felcher, working with Dr. Woodyatt,[7]

7. With the permission of Dr. Woodyatt these data are published.

found that Haines' test gives a positive reaction readily with a concentration of sugar in the urine exceeding 0.07 per cent when 5 c.c. of the reagent and 2 c.c. urine are used.

As in the case of adults, as demonstrated by Benedict, Osterberg and Neuwirth, and of infants, as shown by Greenthal, this urinary sugar can be separated into a fermentable and a nonfermentable portion.

NECROPSY FINDINGS IN NEW-BORN INFANTS*

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Postmortem examinations and the correlation of the findings with clinical phenomena have played a most important rôle in the progress and development of medical science. But only too often the interest in necropsies does not include those performed on new-born infants; instead, deaths in infancy occupy a place similar to the tonsil or appendix in the tissue laboratory, i. e., not examined except under some very important or unusual conditions.

In a previous report [1] I published a survey of routine necropsies performed on new-born infants dying at the University Hospital over a period of three years—a series of thirty-six—in which survey special attention was devoted to the incidence of cerebral hemorrhage. So much interest has been aroused concerning other causes of death that another and more general study from that point of view has seemed advisable. Consequently, a survey of the results obtained in the postmortem examination of infants has been made from the past ten years' record of the department of pathology, including those from the University Hospital. These necropsies were performed by members of the department at the request of various clinicians in various parts of the city, and thus represent not entirely routine examinations but largely those to which some especial clinical interest in regard to either mother or child was attached. Performed as they were by various members of the staff, both past and present, at various times and places and under very different conditions, they lack uniformity in both technic and report of findings. Also in many cases the clinical data were inadequate or unavailable. However, enough significant facts are apparent to stimulate further interest in autopsies on infants and to justify efforts to obtain an examination of every case of death even in infancy.

This series includes 200 necropsies performed on babies who were stillborn or who died a week after birth, thus eliminating to a certain extent postnatal affections. Unfortunately, of the 200, only 136 represented complete examinations, the opening of the skull having been omitted in sixty-three and only the head having been examined in one

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* From the Department of Pathology, University of Minnesota.

1. Warwick: Cerebral Hemorrhage of the New-Born, Am. J. M. Sc. **158**: 95, 1919.

case. Of the total number, 120 were males, seventy-eight were females and the sex was not mentioned in two. One hundred and fifty-two were apparently full term infants, and of these, two (both of whom were stillborn) had a history of having been overdue for about two weeks. Of these full term babies ninety-three were alive at the time of birth; fifty-nine were dead. Forty-eight were probably premature, varying in age from 6 to 8½ months, and of these nineteen were stillborn and twenty-nine lived for some time. Therefore, of the total number, 122 breathed spontaneously and seventy-eight were born dead.

One group of fourteen cases has not been given detailed consideration since they were all coroner's cases representing infanticide and showing evidence of traumatic death unaccompanied in each case by any other evidence of diseased conditions. In yet another case a craniotomy had been performed during a markedly prolonged labor, thus placing this infant in the group of traumatic deaths.

Table 1.—Necropsies Made, Viability of Infants and Lesions Found

		A. Number Done	Per Cent.
Complete necropsies		136	68
Head not examined		63	31
Body not examined		1	0.5
Total		200	
	B. Viability		
Infants living		122	61
Full term	93		
Premature	29		
Total	122		
Born dead		78	39
Full term	59		
Premature	19		
Total	78	200	
		C. Findings	
Lesions found		140	70
Traumatism		14	7
No lesions found		46	23
Head not examined	22		
Premature	16		
Full term	30		
Total	68	200	

In only forty-six of the 200 cases was no gross or microscopic lesion found, but of these forty-six cases the head was not examined in twenty-two, thus rendering impossible the demonstration of some intracranial lesion, such as cerebral hemorrhage—a very frequent finding in newborn infants. Therefore, in only twenty-four of the 200 (12 per cent.) did a complete examination fail to show some demonstrable lesion. In

some of these, premature birth alone might readily have accounted for death; or, there might have been lesions present which were overlooked by the ordinary routine examination. For example, some observers have found that in certain cases the thymus may be so large as to cause very marked compression of the trachea, thus seriously interfering with or preventing breathing. Such a condition, especially when, as often happens, the thymus is not carefully examined, might be overlooked, unless the pathologist is especially well trained.

However, in this series 154 cases, or 77 per cent., did show definite pathologic lesions, even though the examinations were incomplete in some cases. Surely this fact demonstrates beyond a doubt the importance of necropsies on infants, and shows the fund of knowledge which may thus be given to the pediatrician, obstetrician and pathologist. Such a prospect is worthy of the closest cooperation between these specialists and the resulting trend toward more and better scientific medicine.

TABLE 2.—CEREBRAL HEMORRHAGE

			Per Cent.
Stillborn	9	12	
Full term	3		
Premature	3		
	12		
Living		41	
Full term	34		
Premature	7		
	41	53	43
Associated with hemorrhagic disease		20	

Here, as in the shorter series from the University Hospital, the most common finding was cerebral hemorrhage, which occurred in fifty-three cases (Table 2). In the total series only 138 heads were examined, and of these thirteen were those of obviously healthy infants, the victims of infanticide, and therefore only 125 heads were examined in babies dying from natural causes.

Therefore, the fifty-three cases of cerebral hemorrhage found represent a percentage of 42 in all cases of infants either stillborn or dying in the first few days of life, on the bodies of whom a complete examination was made. This number representing, as it does, only cases picked at random by clinicians especially interested in that particular case, compares very favorably with the higher number of 50 per cent. obtained by routine complete necropsies at the University Hospital. In that study it was found that cerebral hemorrhage in the new-born usually presented no distinctive symptoms or syndrome. Therefore,

there are undoubtedly many babies who died because of that condition and yet during life did not attract sufficient attention to justify request for a necropsy or even with a necropsy to make imperative the examination of the brain. It is quite reasonable to conclude that very many of these cases escape a correct diagnosis.

Such figures as these emphasize strongly the attention due such a condition and the value of statistics based on detailed complete and routine postmortem examination of every infant, either stillborn or dying in early infancy. Such a procedure is simplified by the ease with which these permissions are obtained. In many cases, especially in stillbirths, the parents do not require the return of the body following the necropsy. However, even when they do, restoration may be made as satisfactory as in an adult.

Cushing [2] and Strachauer [3] both advise operation as a therapeutic measure in cerebral hemorrhages of the new-born whenever the diagnosis can be made and thus prevent various palsies which may result later in life. In addition, then, to the contribution to general knowledge necropsy studies as to frequency, size and location of these cerebral hemorrhages will be a very real and important aid to the surgeon and may greatly widen his scope of activity in cerebral surgery of the newborn.

It is of great interest to find that of the fifty-three cases showing intracranial hemorrhages, only twelve were stillborn babies while forty-one breathed for some time. In many cases the histories showed that the babies were perfectly normal at the time of birth, the symptoms, when they were present, not appearing for several days. In twenty of these cases the hemorrhage over the brain was associated with hemorrhages in other organs suggesting the syndrome known as hemorrhagic disease of the new-born, which is characterized by an increased clotting time of the blood. This at once brings up the question of the decreased coagulability of the blood being intimately associated with the etiology of the cerebral hemorrhage. One is justified in such an assumption when one finds that nearly one-half of the cases of intracranial hemorrhage are associated with multiple hemorrhages in other organs.

Even in a short, normal labor there must necessarily be great congestion, distortion and, perhaps, laceration of the intracranial blood vessels of an infant. This is emphasized by the anatomic fact that, at this early age, there are no adhesions between the dura and cortex, leaving the delicate blood vessels entirely unprotected as they leave the

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2. Cushing: Intracranial Hemorrhage of the New-Born, Am. J. M. Sc. **130**: 563, 1905.

3. Strachauer: Surgical Treatment of Cerebral Hemorrhage in the New-Born, Minnesota Med. **3**:577, 1920.

surface of the brain. It is reasonable to believe that, although injury frequently occurs, the hemorrhage is small, soon ceases and is finally absorbed in a normal infant. But should the coagulation time of the blood be increased, the hemorrhage may attain great size and finally cause either death or the distressing palsies or contractures too often appearing later in life.

From these findings, as well as those of the former shorter series, one is convinced of the fact that intracranial hemorrhage is a common condition in new-born infants and is often associated with and frequently caused by hemorrhagic disease in the new-born. Further complete routine postmortem examinations on every dead infant will add valuable knowledge to our conceptions of both these conditions as well as their relationships to each other.

TABLE 3.—HEMORRHAGIC DISEASE AND SINGLE HEMORRHAGE

			Per Cent.
A. Hemorrhagic Disease			
Associated with cerebral hemorrhage		20	10
Associated with congenital syphilis		7	3½
Associated with malformations		4	2
Associated with ulcerations		3	1½
Duodenum	1		
Hard palate	2		
Occurring alone		7	3½
Total		41	20½
Clinical symptoms	13		
Head not examined	5		
B. Cases Showing Single Hemorrhage			
Lungs		5	2½
Liver		2	1
Thymus		1	½
Suprarenal		1	½
Total		9	4½

The lesion ranking second to cerebral hemorrhage, both in numbers and importance, is hemorrhagic disease of the new-born considered as an entity by itself. This most important condition has recently been brought into great prominence by Rodda [4] in his study dealing with diagnosis by means of routine determinations of coagulation of the blood carried out by his simple method and, when found, treatment of the disease by means of subcutaneous injections of whole blood.

In this series, forty-one, or 20 per cent., gave evidence of this condition (Table 3), and of these forty-one, only thirteen showed the clinical sign of prolonged bleeding from an abrasion or hemorrhage

4. Rodda: Studies with a New Method for Determining the Coagulation Time of Blood in the New-Born, Am. J. Dis. Child. **19**:269 (April) 1920.

from the mucous membranes. But doubtless had a coagulation time been done the clinical diagnosis would have more closely approximated the autopsy diagnosis.

Of the forty-one bodies showing the multiple hemorrhages, twenty, or one-half, showed also intracranial hemorrhages as mentioned above. In five cases no examination of the brain was made, so had more complete necropsies been performed a yet larger number might have shown hemorrhage over the brain. Since about one-half of the cases of hemorrhagic disease showed cerebral hemorrhage, there is very strong evidence that in many cases the two conditions must be very closely related.

In only seven of these forty-one was there evidence of syphilis. Only four were associated with malformations or developmental defects. This observation is of interest only in the consideration of the possibility of hemorrhagic disease coming under the head of developmental defects and, therefore, being associated with other malformations—a supposition not borne out in this study.

Of great interest, however, is the finding in three of these cases, and in no others in the series, of ulcerations of the mucous membranes from which there was apparently prolonged bleeding judged by the adherent thrombi. One of these ulcers was in the hard palate, the other two ulcers were in the duodenum. One is accustomed to seeing duodenal ulcers associated with hyperacidity in adults but duodenal ulcers in infants is a rare finding. However, since no similar findings were observed in other cases, and since these three cases showed multiple hemorrhages in the viscera as well as clinical signs of bleeding from the mouth and bowel, one is justified in the belief that the ulcerations were the results of the pre-existing hemorrhagic diathesis. This theory is strengthened by the fact that these infants lived three, four and five days, respectively.

Nine other bodies revealed large hemorrhages in single organs—five in the lung, two in the liver, and one each in the thymus and suprarenal. But these cases were not included in the list showing the hemorrhagic syndrome because of the strong possibility of single hemorrhages being due to trauma resulting from birth or artificial respiration.

The next group claiming attention is the ever interesting one of malformations. Of the 200 cases studied, thirty showed developmental defects, and in only eight of the thirty were multiple malformations noted. Therefore, contrary to the belief that malformations usually are multiple, less than one-quarter of the cases of this series followed that rule (Table 4). The majority of these are listed in the table and need no farther explanation. Many of the more common ones appear but once. The case of transposition of the viscera was complete in every detail. Polycystic kidney occurred twice and both were extreme cases. Each one showed a normal liver. Two most striking anomalies of the

TABLE 4.—MALFORMATION

		Per Cent.
Heart		
Opening in interventricular septum	4	
Very large opening in interauricular septum	1	
Bifid apex	1	
Four cusps on aortic valve	1	
Absence of interventricular septum and pulmonary artery	1	
Pulmonary artery continuous with aorta	2	
Atresia of pulmonary vein	1	
Aorta of pulmonary from right ventricle	1	
Total	12	6
Gastrointestinal tract		
Atresia of small intestine	4	
Stricture of esophagus	2	
Subhepatic position of colon	1	
Total	7	3½
Urinary tract		
Absence of right kidney, ureter, urethra and anterior abdominal wall	1	
Double kidney and ureter	1	
Atresia of ureters at bladder orifice	1	
Hydronephrosis and hydroureters (bilateral)	3	
Hydronephrosis and hydroureter (unilateral)	1	
Horseshoe kidney	1	
Malformed kidney	1	
Polycystic kidney	2	
Total	11	5½
Liver		
Hemangioma	1	
Malformed liver	1	
Total	2	1
Suprarenals		
Accessory suprarenal	1	
Aplasia of suprarenals	1	
Total	2	1
Brain and spinal cord		
Hydrocephalus	2	
Iniencephaly	1	
Anencephaly	1	
Encephalomeningocele	1	
Encephalocystocele	1	
Spina bifida with hydrocephalus	2	
Total	8	4
Transposition of viscera	1	
Cleft palate	1	
Hare lip	1	
Club feet	1	
Accessory spleen	1	
Stenosis of larynx	1	

Total cases, 30.
Multiple, 8.

heart were seen; one case showing only one single large ventricle and leading from it one large artery which gave off branches to the lungs and then followed the usual aortic course. The other had a blind end to the pulmonary vein and no vessels communicating with the left ventricle, the only opening being in the interventricular septum. The other malformations of the heart were those which are usually seen.

Atresia of the small intestine was observed four times. In each case there was no complete interruption of continuity, but a solid cord connected the two patent ends of bowel. One of these cords was found in the lower end of the small intestine at a point corresponding to the frequent site of a Meckel's diverticulum; in a second case the cord was at the junction of duodenum and jejunum; in a third, it was 75 cm. below the pylorus and was associated with a definite break in the mesentery; and in the fourth case it was in the duodenum. Congenital stricture of the esophagus occurred twice and stenosis of the larynx once.

TABLE 5.—BIRTH INJURIES

		Per Cent.
Fractured vertebrae (3rd, 4th and 5th)	3	
Fractured skull	1	
Dislocated occipital bone	1	
Torn tentorium	1	
Ruptured mediastinum	1	
Total	7	0.3½

There was a comparatively large number of malformations of the head and spinal cord, due, perhaps, to the fact that these were unusual, attracted attention and were sent to the university because they were thought to be of special interest. The percentage of necropsies on such cases is, therefore, much higher than would result from routine examinations of every dead infant.

For the same reason, there are a large number of birth injuries. A long, abnormal or otherwise unusual labor resulting in a stillborn child or one dying soon after birth excites the interest and suspicion of both the obstetrician and the relatives, and a necropsy is requested. In this series birth injuries were seen seven times (Table 5). The most common injury was fracture of the vertebrae, which occurred three times in the third, fourth and fifth vertebrae, respectively, and in each case, as would be expected, there was a laceration of the spinal cord at that level. A fractured skull was seen only once, as was also one case of dislocation of the occipital bone causing a fatal hemorrhage, one example of a tear in the tentorium, and one instance of a ruptured mediastinum with resulting emphysema and pneumothorax. However, even considering the number of birth injuries as being larger here than

in routine series, it is still very small, representing as it does less than one-half of 1 per cent.

Congenital syphilis was found twenty-three times, and in only thirteen cases were signs or symptoms in the parents given in the history. However, it must be borne in mind that the majority of these histories were obtained by the pathologist under adverse conditions, and are consequently, in many instance, at least, neither complete nor reliable. On the other hand, in eight cases the parents gave signs of syphilis but no demonstrable evidences of syphilis were found in the necropsy on the child. In this latter group the infants might have escaped the disease, although in some cases, at least, the presence of the disease may have been overlooked or may have been in a latent form. Syphilitic lesions frequently do not stand out very prominently and may appear only in the microscopic picture, and only too often this is complicated or obscured by the pronounced autolysis or postmortem changes having taken place either before or after birth. An examination of the epiphyseal line may be of definite value, but cannot always be carried out without an unwarrantable mutilation of the body. Congenital syphilis may easily be overlooked unless a careful and detailed search be made on a body which has not yet undergone too marked postmortem changes.

It is of interest to note that in the nineteen cases showing evidences of congenital syphilis, only two bodies were in a macerated condition, while nine other bodies without either findings or history of syphilis showed maceration. While it is an undisputed fact that causes other than syphilis may produce death of the fetus in utero, it must be admitted that in many instances maceration may have obscured the evidence of syphilis, and that since many of these histories were incomplete or inadequate the condition may have been really present in a larger percentage of cases than is shown by this analysis.

In such a series as this, consisting of infants dying within a week of birth, very few acute infections were found. In the case of one baby, living six days, death was caused by infection of the umbilical stump. In the case of another baby living only twelve hours, a marked vegetative mitral and tricuspid endocarditis was found. Since the infant showed evidences of congenital syphilis and the mother gave a history of a recent rash typical of the secondary stage of syphilis, this was considered to be an acute syphilitic lesion of the heart valves. However, as there had been no opportunity at this necropsy to make careful bacteriologic studies, the possibility of this being a streptococcic infection superimposed on a syphilitic condition must be considered. Another possibility is that these apparent vegetations were only subendocardial hemorrhages on the edges of the valve leaflets—a condition described at length in the literature but not observed in any cases in this series.

Another baby living only two days and showing a marked jaundice after birth, presented at necropsy a definite abscess of the liver and acute splenitis. Since such a condition probably could not have developed in two days, this points strongly toward a hematogenous infection from the mother, who must have had at least a transitory bacteremia.

TABLE 6.—CONGENITAL SYPHILIS

		Per Cent.
A. Findings		
Associated with hemorrhagic disease	5	
Associated with cerebral hemorrhage	3	
Associated with bronchopneumonia	1	
Alone	11	
Total	19	9½
B. Viability		
Living	11	
Dead	8	
Macerated, 2.		
Total	19	9½
C. History		
With history in parents	13	
Without history	6	
Total	19	9½
History in other cases without findings, 8.		
Body macerated without syphilis, 9.		

TABLE 7.—ACUTE INFECTIONS

Bronchopneumonia	4
Infected umbilical stump	1
Endocarditis (mitral and tricuspid)	1
Abscess of liver with splenitis and hepatitis	1
Total	7

A fourth baby showing evidences of congenital syphilis presented also a bronchopneumonia which did not at all resemble the "white" or syphilitic pneumonia. This child had lived seven days and, undoubtedly with a lowered resistance due to the syphilitic condition, early fell a prey to bacterial infection of the respiratory tract.

One case of especial interest was that of a full term infant who lived only two and one-half hours and presented at necropsy a very typical bronchopneumonia. Smears from the lung showed polymorphonuclear leukocytes and gram-positive cocci in pairs and chains. There is little doubt that this condition also developed in utero, although the mother appeared to be entirely normal. A fourth case of bronchopneumonia was found in an infant who lived three days and whose temperature reached 102 F. In this instance the mother, at the time

of delivery, was suffering from a severe attack of tonsillitis. These cases demonstrate very well the occurrence of infections contracted either in utero or at the time of birth.

Another infant apparently normal at birth, at three days of age developed a temperature of 105 F. and died the following day. The necropsy revealed a peculiar hemorrhagic process involving the greater part of both lungs. This picture was practically identical with the so-called "hemorrhagic bronchopneumonia" seen so frequently in patients dying of influenza. Since this occurred at the early outbreak of the 1918 influenza epidemic, it was probably an instance of this disease in a new-born infant—an uncommonly rare occurrence.

Another case of interest as an example of acute infection in the new-born has already been reported by Barron [5] but was excluded from this series because the infant lived eleven days. This was a case of cerebrospinal meningitis caused by a strain of *B. coli*.

TABLE 8.—SUMMARY

Cases examined	200	Per Cent.
Complete	136	
Traumatic deaths	15	7½
Cerebral hemorrhage	53	44
Hemorrhagic disease	41	20½
Malformations	30	15
Birth injuries	7	3½
Congenital syphilis	19	9½
Acute infections	7	3½

It would be of interest in this series, especially in those mothers showing no evidence of disease, to know how long before delivery the rupture of the fetal membrane took place. Early rupture of the membranes, as well as vaginal examinations, suggest a possible etiology for infections present in the infant at the time of birth.

In two cases only of the series did the cranial bones show ossification with practical obliteration of the fontanels. Partial atelectasis of the lungs seemed to be a common finding even in infants breathing spontaneously, but in three babies living for some time it was very marked and constituted the only lesion found. In these particular infants there must have been some as yet unrecognized factor preventing the normal expansion of the lungs and causing death by improper aeration.

Small hemorrhages under the pleura and epicardium were so common in this series that they cannot usually be considered more than terminal phenomena. In the majority of the cases also the foramen ovale was incompletely closed and the ductus arteriosus was entirely or partially patent.

5. Barron: Meningitis in the New-Born and Early Infancy, Am. J. M. Sc. **156**:358, 1918.

Just as this survey proves most conclusively the importance of performing a necropsy on every dead infant, it also shows that in order to obtain results of definite and permanent value each necropsy should be performed by a trained examiner. In many cases the lesions found in a new-born infant differ very markedly from those of the adult, e.g., the frequent occurrence of hemorrhages of the brain or developmental anomalies, such as patent foramen ovale and ductus arteriosus, etc. In the hands of an untrained observer such lesions as are often present in infants may either escape notice altogether or have placed on them undue significance in relation to the cause of death. Therefore, in order to obtain the most complete necropsies and to have uniformity in the reports, the specialization of one member of the pathologic staff in infant necropsies is most advisable. That such a member be also interested in the clinical field of pediatrics offers attractive possibilities. Such an arrangement has already been attempted at University of Minnesota, where a teaching fellow in pediatrics is also a member of the pathology staff. In addition to his clinical work he offers an elective in infant pathology, helps establish a branch museum of specimens from the new-born and also attempts to attend every postmortem examination on infants. Under such conditions these necropsies take on new significance and importance and stimulate the clinicians to greater activity in obtaining permissions and to greater interest, shown by attendance and frank discussion at the autopsy table. This interest is usually shared by pediatrician, obstetrician and pathologist, thus leading to a cooperation which renders possible an extension of medical knowledge in a field often neglected, and promotes that ideal of all medical work, the conservation of human life and health.

SUMMARY

1. Careful, complete, routine necropsies performed on all dead infants will return very valuable knowledge to the pediatrician, obstetrician and pathologist.

2. Cerebral hemorrhage is a common condition in new-born infants, occurring in from 43 to 50 per cent. of those examined.

3. Hemorrhagic disease of the new-born is also a frequent finding and is often associated with cerebral hemorrhage.

4. Malformations occurred in 15 per cent. of which only 4 per cent. were multiple. Of these, developmental defects of the heart were most common but those of the digestive tract were surprisingly numerous.

5. Birth injuries were rare (0.7 per cent.) but when they occurred they were usually in the spinal column.

6. Congenital syphilis is frequently diagnosed with difficulty, especially in the case of fetuses dead some time before birth.

7. Acute infections were rare; bronchopneumonia was the most frequent.

A CASE OF MENINGOCOCCUS MENINGITIS WITH OBSTRUCTIVE HYDROCEPHALUS IN THE NEWLY BORN *

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Although meningococcus meningitis is a common disease in later infancy and childhood, it is extremely rare during the first two months of life. In a careful review of the literature, I have been able to find reported only six cases of meningococcus meningitis occuring in infants under 2 months of age, only one of these having associated obstructive hydrocephalus. There are reported twenty-eight cases of meningitis due to organisms other than the meningococcus occurring in infants under 2 months of age. The causative organisms, and ages are shown in Table 1.

TABLE 1.—ANALYSIS OF MENINGITIS CASES AS TO CAUSATIVE ORGANISMS AND AGES OF PATIENTS

Organism	Age	Total
Colon bacillus	Newly born (3); 3 days; 8 days; 9 days; 11 days; 16 days; 4 weeks (2); 6 weeks	11
Staphylococcus and streptococcus	Newly born (6); 6 weeks (2); 7 weeks	9
Meningococcus	Newly born; 2 weeks; 29 days; 5 weeks; 6 weeks; 2 months	6
Pneumococcus	Newly born; 3 days; 3 weeks; 8 weeks	4
B. lactic aerogenes	8 days	1
B. mucosus capsulatis	6 days	1
B. pyocyaneus	8 days	1
Micrococcus catarrhalis	39 days	1
Total		34

REVIEW OF LITERATURE

Meningococcus Cases.—Holt,[1] in a discussion of 300 cases of meningitis in infancy and childhood mentions one case of meningococcus meningitis in an infant 5 weeks of age. This patient died of marasmus after all acute symptoms had subsided.

Koplik,[2] in an article on meningitis in the newly-born and infants up to 3 months of age, reports two cases. One of the two patients, in the newly-born, was cured of the acute symptoms. This patient later developed a moderate hydrocephalus. The second patient, aged 6 weeks, died after an illness of one week.

Miller[3] reports a case of meningococcus meningitis in an infant aged about 2 weeks. The infant died on the fortieth day. In this case the symptoms of

* Received for publication, Jan. 26, 1921.

1. Holt, L. E.: Observations on Three Hundred Cases of Acute Meningitis in Infancy and Childhood, Am. J. Dis. Child. **1**:26 (Jan.) 1911.

2. Koplik: Meningitis in New-Born and Infants Under Three Months of Age, Arch. Pediat. **33**:481, 1916.

3. Miller, D. J.: Case of Meningococcus Meningitis in New-Born with Interesting Unusual Features, Arch. Pediat. **34**:824, 1917.

meningitis were not at all definite until a few days before death. Necropsy showed suppurative meningitis more marked over the sulci and at the base than elsewhere over the brain.

White[4] cites one case in an infant, aged 29 days. Repeated lumbar puncture produced only a few drops of fluid at times, none at other times; therefore, the diagnosis of acute hydrocephalus with obstruction was made. The infant was treated with intraventricular injections of serum, 180 c.c. in all being given. The infant recovered from the acute illness and died at 11 months showing an extreme hydrocephalus.

Haushalter and Remy,[5] in reporting a series of 272 cases of meningitis, mention one case of meningococcus meningitis in an infant aged 2 months. No particulars about the case were given.

Cases of Meningitis Other Than Those Caused by the Meningococcus.—Sherer[6] reports three cases of meningitis in infants aged 8 days, 9 days and 6 weeks, respectively. Necropsy in all three cases showed fibrinopurulent meningitis with bilateral otitis media, the organism in each case being the colon bacillus.

Hinsdale[7] describes a case of meningitis in an infant 3 days old, caused by *B. coli immobilis.* Necropsy showed a brain abscess in the left frontal lobe with exudate on the surface. He states that at birth pus came from the uterus of the mother during and after expulsion of the placenta.

Shieb[8] reports a case in an infant 8 days old caused by *B. lactis aerogenes* The diagnosis was made at necropsy, which showed a purulent meningitis.

Goldreich[9] records a case of antenatal infection with colon bacillus. The patient showed symptoms of meningitis on the first day of life, and died on the second. Necropsy revealed purulent meningitis, pleuritis and bronchitis.

Benfey[10] reports a case of *B. pyocyaneus* meningitis in an infant, aged 7 days. The patient died on the eighth day. There was an inflammation of the umbilicus.

Noeggerath[11] reports a case in a 16 days old infant caused by *B. coli immobilis capsulatus.*

Holt[1] also speaks of two cases of coli meningitis in infants 4 weeks old, and six cases of staphylococcus and streptococcus meningitis in the newly-born.

Bonhoff and Esch[12] report a case in an infant, 6 days old dying on the fourteenth day, due to *B. mucosus capsulatus.* Necropsy showed pus over the brain and an otitis media of the right side.

Michael[13] cites a case of colon meningitis in the new-born reported by Von Reus, no reference being given in his bibliography.

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4. White, T. W.: Infectious Meningitis Developing in Babies from Twenty-Nine to Thirty Days Old. Case Reports, Arch. Pediat, **34**:372, 1917.

5. Haushalter and Remy, A.: Statistique dés meningitis observées á la Clinique des Enfants d'un mois à 12 ans, Rev. méd. de l'est. **45**:533, 1913.

6. Sherer: Ein Beitrag zur Aetologie der Leptomeningitis Purulenta bei Säuglingen, Jahrsb. f. Kinderh. **39**:1, 1895.

7. Hinsdale: Purulent Encephalitis and Cerebral Abscess in New-Born Due to Infection from the Umbilicus, Am. J. M. Sc. **118**:280, 1899.

8. Schieb: Prag. med. Wchnschr., **5**:169, 1900.

9. Goldreich: Meningitis beim Neugeborenen, Jahr. f. Kinderh. **56**:808, 1902.

10. Benfey: Ueber Pyozyaneussepsis, Med. Klin. **50**:1199, 1907.

11. Noeggerath: Bacillus Coli Immobilis Capsulatus bei Einem Falle von Eitrigen Meningitis Cerebrospinalis, München. med. Wchnschr. **54**:617, 1907.

12. Bonhoff and Esch: Ueber Einem Fall von Meningitis purulenta beim Neugebornen infolge rechtseitiger Mittleohrentzündung, Ztschr. f. Geburtsh. u. Gynäk., **70**:886, 1912.

13. Michael: Recovery of Colon Bacillus from Spinal Fluid of Five Months Infant, Arch. Pediat. **33**:280, 1916.

Herman[14] reports a case of pneumococcus meningitis in an infant, aged about 3 weeks, saying that his case is the first one reported up to 1915. The infant died without symptoms of meningitis. Necropsy showed a thick yellow exudate on the anterior surface of the brain, and increased ventricular fluid.

Koplik[2] also reports three cases of streptococcus meningitis in infants aged 6 weeks (two cases), and 7 weeks (one case); one case of colon bacillus meningitis in a new-born; and two cases of pneumococcus meningitis, one an infant aged 8 weeks, and one in the new-born.

White,[4] in addition to the case already cited, reports a case in an infant aged 39 days, due either to the meningococcus or the *Micrococcus catarrhalis*. The infant died after an illness of thirty days. Necropsy showed dilated ventricles with membranous exudate.

Barron[15] finds in a review of the literature only thirty-nine cases of meningitis in infants under 3 months of age, nineteen of these being in the new-born. He adds one case of his own in an infant, aged 11 days, due to the colon bacillus. Necropsy showed fibrinopurulent exudate over the brain.

L'Esperance[16] reports a case of pneumococcus meningitis in an infant, aged 3 days. The baby died on the sixth day.

In the cases here reviewed, obstructive hydrocephalus was observed during the acute disease in only one case. All of the cases, other than those due to the meningococcus, ended fatally, while of the six meningococcus cases, two patients died during the acute stage of the disease; one died later as a result of the development of hydrocephalus; one died of marasmus after all symptoms of meningitis had subsided; one recovered with a moderate degree of stationary hydrocephalus, and in one case the termination of the disease was not mentioned. The symptoms were at first obscure in the majority of cases, and indeed, the diagnosis was made only at the necropsy in several instances.

The findings in the following case seen in Dr. Howland's service at The Harriet Lane Home illustrates meningococcus meningitis with obstructive hydrocephalus, discovered at the age of 5 weeks, probably acquired at birth, or shortly thereafter. Definite symptoms were first observed at the age of about 2 weeks, but so obscure were these symptoms that it was not thought necessary for a physician to see the infant until he was almost 5 weeks old.

REPORT OF CASE

Baby C., a male infant, aged 5 weeks, was admitted to The Harriet Lane Home, May 22, 1919.

Family History.—Mother living, aged 22 years; has had almost constant indigestion and been very nervous since child's birth, otherwise well. Father, living and well, aged 25 years. There were no stillbirths or miscarriages. No

14. Herman, C.: Meningitis in New-Born with Report of a Case, Arch. Pediat. **33**:384, 1915.

15. Barron, M.: Meningitis in New-Born and Early Infancy, Am. J. M. Sc. **156**:358, 1918.

16. L'Esperance: Meningitis in an Infant Six Days Old, Med. Rec. **97**:548, 1920.

children have died. Patient, second child; one other, a girl 3 years old, living and well. No history of syphilis. There was a possibility of tuberculosis in paternal grandmother.

Previous History.—Born at full term, normal delivery; birth weight 7 pounds. Appeared to be a normal healthy baby at birth. No jaundice, hemorrhages, snuffles or convulsions at birth. Was breast fed eleven days irregularly, then because of nervousness of mother, green stools, fretfulness, and irritability of baby was put on a condensed milk mixture. Did not do well on this, so was again placed on breast, to be changed again to condensed milk because of vomiting and failure to gain in weight.

Present Illness.—Since birth the infant appeared to be very nervous, twitching at slightest provocation; was also very irritable. He had always cried a great deal. Shortly after birth, the parents thought they noticed slight retraction of the head, although they were rather indefinite as to when they were sure of this condition. They also thought the fontanel had always been full. At the age of 10 days, a diffuse mottled rash appeared, lasting two days, which the parents took to be measles. At this time also the baby began to spit up some of his food, and thrush was noticed, which persisted for some time. Occasional attacks of fever then began, and the retraction of the head and tense fontanel were said to be definite. From then until the infant was 33 days old, the same symptoms existed, only growing steadily worse. The first real convulsion occurred on the thirty-third day, and vomiting became quite pronounced. Convulsions and vomiting were persistent from then until admission to the hospital four days later.

Physical Examination.—Measurements: Head, 37.5 cm.; chest 31 cm.; abdomen, 30 cm.; length, 42 cm. The general appearance is that of a poorly nourished and developed and apathetic appearing white boy, lying quietly in bed when not undergoing a convulsion or twitching. He cannot be made to cry, but at the slightest movement twitching occurs. The skin shows occasional petechiae on the body and extremities. The head is large symmetrical; fontanels are both wide open and bulging. The sutures are separated. No craniotabes. The eyes are rolled upward with each convulsion, but between times show occasional vertical nystagmus. No strabismus. Pupils are equal, regular in outline, and react to light. Conjunctivae are slightly injected. Sclerae are clear. There is a slight purulent discharge from both eyes. The ears show no secretion or mastoid tenderness. There is a mucopurulent secretion from both nostrils, no obstruction. Tongue is slightly red, with whitish coat, moist. Tonsils and pharynx are slightly injected. Respirations are rapid. Lungs show no impairment of resonance. Breath sounds are normal. The liver and spleen are both barely palpable. The knee jerks are equal and lively; no Babinski; Kernig questionable on both sides, biceps and triceps present and equal. Superficial reflexes not obtained. There is marked rigidity of the neck. The external genitalia are normal. Otoscopic examination shows both ear drums normal. Ophthalmoscopic examination shows a choked disk on both sides.

Laboratory Examination.—White blood count, 18,000. Von Pirquet test negative. Urine shows slightest possible trace of albumin, no sugar; sediment shows amorphous urates only.

A lumbar puncture done on admission yielded 4 c.c. of brownish cloudy fluid, obtained drop by drop, with difficulty. The fluid showed positive globulin (Pandy), many leukocytes, the majority being polymorphonuclears, with also a considerable number of endothelial cells. No organisms were found in smears from this fluid, and cultures were all negative. A ventricular puncture done at this time yielded cloudy fluid under increased pressure. Twenty c.c. were removed from the right ventricle and 10 c.c. of serum were introduced. A smear from this fluid showed many cells, mostly polymorphonuclears, with an abundance of gram-negative intracellular and extracellular diplococci. Cultures showed the meningococcus.

Clinical Course.—May 23: Temperature, 103 F.; pulse, 160; respiration, 52. The infant appeared slightly better. Convulsions had ceased, although twitching of the lips and hands continued. Took feedings well; no vomiting. Temperature and pulse higher than on the previous day. A ventricular puncture was done in the morning, 45 c.c. of fluid being removed and 40 c.c. of serum given. A lumbar puncture done in the afternoon gave identical results as on the previous day, also 10 c.c. of serum were introduced this time. The infant showed no ill effects from the punctures. Another ventricular puncture was done at 10 p. m., in the left ventricle, 45 c.c. of fluid being removed and 20 c.c. of serum introduced. The number of organisms seen in smears from this fluid was greatly diminished and cultures gave scanty growth. The patient became slightly cyanotic after this puncture and vomited. The reaction lasted only a few minutes, however. Temperature rose to 106 F. two hours after the puncture, falling again in the following two hours to 102 F.

May 24. Temperature, 103 F.; condition about the same as on the previous day. A lumbar and ventricular puncture were done in the afternoon. Only 4 c.c. were again obtained by lumbar puncture. Forty c.c. of fluid were withdrawn from the ventricle, and 20 c.c. of serum introduced. In both fluids the cell count was lower and no organisms were seen in smears, or grew in cultures this time. The ventricular puncture was again followed by cyanosis and slowing respirations, but improvement occurred shortly after a stimulant was given. The improvement was, however, only temporary, the infant again becoming cyanotic, twitching almost continually, and respirations growing slower until they ceased an hour later. Permission for necropsy was refused.

DISCUSSION

The obscurity and irregularity of the symptoms in meningitis of the new-born in the early stage of the disease is admitted by all observers. The most constant symptoms are vomiting (not projectile), extreme restlessness, twitching, (general), convulsions (repeated), later, bulging of the fontanel and retraction of the neck.

Miller's case illustrates this course. The onset was at 2 weeks of age with conjunctivitis and a vesicular eruption on the abdomen. The first definite symptom of meningitis (tremor of the eyelid), occurred at twenty-five days, followed by convulsions and other typical symptoms of meningitis. The infant died ten days later.

Holt and Koplik both remark on the irregularity in the clinical course. Koplik found the temperature high at onset, going to normal or 1 degree above later in the disease. Convulsions, frequently repeated, twitching, restlessness, vomiting and groaning respirations are important symptoms. He found that after a week or more, rigidity of the neck, and bulging fontanel develop. He thinks that tetany and meningeal hemorrhage are two conditions most often confused with miningitis. Tetany, however, occurs in later infancy (from 6 months to 2 years). In the cases of meningeal hemorrhage, there is no fever, convulsions are not repeated, the fontanel has a boardlike feel with no pulsation, and does not become prominent as the disease progresses.

In the case here reported, the infant was not seen until the symptoms were quite definite. He showed at this time a temperature of

103 F., frequent convulsions, twitching, vomiting (not projectile), bulging fontanel, retracted neck, very large head with separated sutures, and questionable Kernig. The parents stated that he had been restless and irritable since birth. The first symptom was a mottled rash at the age of 10 days. This was followed in a few days by thrush, and from then on occasional attacks of fever. At 2 weeks of age, slight retraction of the head was definitely noted, and vomiting began at this time. The vomiting was not severe, however, until the infant was 4½ weeks old. The first convulsion occurred on the thirty-third day, and the child was brought to the hospital on the thirty-fifth day. The fact that the head was so large in size with separated sutures, that there was a choked disc on both sides, but especially that only a few drops of fluid were obtained on lumbar puncture, while a large quantity was obtained on ventricular puncture, establishes the diagnosis of obstructive hydrocephalus associated with the meningitis.

SUMMARY

Meningococus meningitis in the new-born and early infancy is rare. Only one case of meningococcus meningitis with obstructive hydrocephalus developing during the acute stage of the disease was found in the literature.

The symptoms are usually irregular and obscure. The most important ones are repeated convulsions, vomiting (not projectile), and after a week or more, bulging of the fontanel and rigidity of the neck.

PROGRESS IN PEDIATRICS

REVIEW OF THE EAR, NOSE AND THROAT LITERATURE FOR THE YEAR 1919*

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As might have been expected, the literature for 1919 is full of articles of a military nature having but little bearing on the work of a pediatrician. In addition to this most of the foreign journals have not found their way to this country.

THE EAR

Dean and Bunch [1] have constructed a pitch range audiometer driven by electricity that covers the range of hearing in ordinary use without a break, enabling one to test out the hearing very rapidly. Both the pitch and the intensity of the tone are under perfect control.

In an article on teaching the deaf child, Goldstein [2] states that more than 2,000 children were attending the public schools of St. Louis, who had some form of speech defect, many of these, no doubt, being the result of defective hearing.

Heilshon observed three patients who had lost their hearing from mumps.

Blackwell [3] divides earache into four classes: (1) Inflammation behind the tympanic membrane, usually preceded by inflammation in the upper air passages; (2) inflammation of the soft parts of the external auditory canal; (3) otalgia, the pain being referred from teeth, nose or throat, and (4) mechanical, occurring mainly in children with enlarged tonsils and adenoids. The pain in this form is nearly always nocturnal.

COMPLICATIONS OF EAR DISEASE

Holmes [4] seems to think that mastoiditis is the same as an abscess anywhere, and that opening is indicated as soon as pus is formed. He says, "It is, therefore, a self evident proposition that to operate at the earliest possible moment is sound surgery and should always be followed." (I believe that most otologists will disagree with this

* Received for publication March 6, 1921.

1. Laryngoscope **29**:453, 1919.
2. Laryngoscope **29**:503, 1919.
3. New York M. J. **109**:1076 (June 21) 1919.
4. Ann. Otol., Rhinol. & Laryngol. **28**:1, 1919.

statement for pus is found in the mastoid in practically every case of acute suppurative otitis media, and if every patient with pus in the mastoid is operated on, it would mean operation for practically every case of acute suppurative otitis media, and since the great majority of cases of acute suppurative otitis media recover without operation, many needless operations would be done if this advice were followed).

Kernan [5] gives the history of a child, aged 5 years, who probably had had influenza three weeks previously, recovering in ten days. Eight days later he became feverish, vomiting on the ninth day. Two days later he entered the hospital with practically negative symptoms. A few days later his neck became rigid with a doubtful Kernig. He was irritable, hyperesthetic, and would not answer questions. He next developed convulsions, nystagmus and left facial paralysis. A mastoid operation was done on the left mastoid and the cerebellum explored. Gas escaped from the wound but no pus was found. The final outcome of the case is not given. In a case reported by Mann,[6] the patient had a right sided cerebellar abscess. When the patient's nose was held, he always used his left hand to brush away the hand holding his nose.

Mollison [7] reports the case of a boy, aged 12½ years, who had scarlet fever at 2. He had a right frontal headache, vomiting, tenderness over the right mastoid and was supposed to have had mumps two weeks previously. His temperature was 97 F., pulse 68. He was drowsy and had photophobia. There was pus in the right ear. A mastoid operation was done on the right side, the right temporosphenoidal lobe was explored and one ounce of pus evacuated. He improved, but the pus reaccumulated and had to be evacuated a second time, following which a hernia cerebri developed. A large part of the hernia was pulled off and was found to consist of the abscess sac. Ophthalmoplegia developed three days later. The patient made a slow but complete recovery.

Borries [8] finds that the cerebrospinal fluid may be sterile, particularly in cases in which the meningitis is an accompaniment of pachymeningitis interna or brain abscess.

Aboulkir [9] classifies meningitis as follows:

(1) Purulent septic meningitis; (2) purulent aseptic meningitis; (3) serous septic meningitis; (4) serous aseptic meningitis, presenting itself under two forms, diffuse and hypertensive. He reports the following cures: Septic meningitis, one patient cured by medical

5. Laryngoscope **29**:322, 1919.
6. Ztschr. f. Ohrenh. **74**:4, 1919.
7. J. Laryngol., Rhinol. & Otol. **34**:161, 1919.
8. Arch. f. Ohrenh., Nasenh. u. Kehlkopfh. **103**:37, 1919.
9. Rev. de l'Or. et d. Rhin., (May 15) 1919.

treatment, one by mastoid operation, and one by mastoid operation with incision of the meninges. Aseptic meningitis—one patient cured spontaneously, six patients cured by mastoid operation, and four cured by mastoid operation with incision of meninges (once with puncture of the ventricle).

The same author [10] says that the classic treatment of intracranial complications of ear diseases is dominated by three principal considerations: (1) Difficulty of diagnosis; (2) necessity of early operation, and (3) necessity of opening the cranium and following osseous lesions and of traversing the mastoid in successive steps.

A number of interesting papers on mastoiditis appeared during the year, and a number of interesting points in the disease were brought out.

Harris,[11] in a paper on ear diseases following measles at Fort Oglethorpe, states that of 1,685 cases of ear disease treated at Fort Oglethorpe, 607 were the result of measles. Usually the ear trouble developed without complaint from the patient and was discovered during routine examination. The rule was to do a paracentesis as soon as any change was discovered in the membrana tympani. Acute mastoiditis appearing in a patient suffering from measles is usually as free from pain as is the otitis media. On account of the great gravity of the mastoid cases, operation was performed under gas-oxygen anesthesia. Of thirty-one patients so operated on, ten had bronchopneumonia and one had mumps. There were no complications and no shock following anesthesia.

Robinson [12] reported a case of toxic delirium following an operation for mastoiditis. The patient became insane with delusions of persecution.

Goldstein [13] reports a series of mastoid operations done under local anesthesia with the minimum of pain and maximum of safety and with 100 per cent. perfect recoveries. (This method of operation should be done more where the patient is very toxic as in scarlet fever, where nephritis is present, or where the patient has pulmonary lesions that may be aggravated by general anesthesia.

Haines [14] reported a case of mastoiditis in a hemophiliac on whom operation was done. It was necessary to do transfusion twice and to use coagulin Ciba. The patient recovered.

Smith [15] considers that mastoiditis occurring in patients with fracture of the skull has a very poor outlook because of the meningitis that is apt to occur. Tilley [16] claims that filling the mastoid wound

10. Rev. de l'Or. et d. Rhin., (March 15) 1919.
11. Ann. Otol., Rhinol. & Laryngol. **28**:50, 1919.
12. Ann. Otol., Rhinol. & Laryngol. **28**:86, 1919.
13. Laryngoscope **29**:559, 1919.
14. Laryngoscope **29**:609, 1919.
15. Laryngoscope **29**:552, 1919.
16. Laryngol., Rhinol. & Otol. **34**:73, 1919.

with a mixture of bismuth subnitrate, iodoform and liquid paraffin, and completely suturing the wound, materially shortens the after-treatment of mastoiditis.

Stickney [17] reported two cases of Gradenigo's syndrome in patients aged 6 and 34 years, respectively, both females. In the child an acute rhinitis was followed by acute suppurative otitis media on the left side and this by paralysis of the left abducens. A simple mastoid operation was done and the diplopia subsided inside of two weeks. In the second case it was necessary to introduce a drain between the dura and the bone almost to the apex of the petrous portion before improvement set in.

Hill [18] had a patient who had spontaneous hemorrhage after a simple mastoid operation. The patient recovered.

McKinley [19] had a case of spontaneous recovery from thrombosis of lateral sinus.

Inhope [20] considers that the patient's chances of recovery after an operation for sinus thrombosis may be put at 50 per cent.

Holmgren [21] uses radium in the treatment of tubal stenosis. Lymphoid tissue, in particular, is particularly susceptible to the influence of radium, and stenosis of the tuba is largely due to lymphoid tissue in its mucosa. His results were satisfactory.

Agazzi [22] says that tuberculosis of the ear does not always occur by way of the tuba, but that it also occurs by way of the circulation.

MOUTH AND THROAT

Canuyt [23] reports a case of noma and advises for treatment the use of stimulants and cardiac tonics, derivatives and intravenous injections of collargol, electrargol and camphorated water. For local treatment he advises caustics, combating local symptoms after separation of the slough. He finds noma rare in France but common in hot countries like Annam where it occurs after eruptive fevers, typhoid fever, pneumonia, diphtheria, etc. Poor nutrition, poor housing and insanitary conditions favor its development. It never occurs in the course of good health. He divides its course into three periods:

1. Invasion: Ulceration of inside of cheek or on gums, or a hard area of induration.

2. Period of progress: Ulceration progresses or multiplies and gangrene sets in. The skin becomes gangrenous in turn.

17. Laryngoscope **29**:90, 1919.
18. Ann. Otol., Rhinol. & Laryngol. **28**:566, 1919.
19. Laryngoscope **29**:13, 1919.
20. Arch. f. Ohrenh., Nasenh. u. Kehlkopfh. **103**:97, 1919.
21. Laryngoscope **29**:590, 1919.
22. Monatschr. f. Ohrenh. u. Laryngorhinol. **48**:676, 1919.
23. Rev. de Laryngol., Otol. et Rhinol. **40**:6, 1919.

3. Period of elimination and repair: Line of demarcation forms, sloughing occurs, to be followed by granulation and healing. In the differential diagnosis are to be considered gangrenous aphtha, ulcero-membranous stomatitis, malignant pustule and malignant syphilis.

Bryan [24] considers all local treatment of tonsils after cultures have shown the presence of *Streptococcus hemolyticus* as not only deceptive, but a waste of time. A complete enucleation is necessary.

Nichols [25] finds that carriers of streptococci are very common—in over half the population.

Moore [26] in an article on hemorrhage after tonsillectomy gives the following sources for the bleeding:

(1) Tonsillar artery; (2) ascending pharyngeal artery; (3) descending palatine artery; (4) ascending palatine artery; (5) dorsalis linguae artery; (6) capillary oozing; (7) enlarged venous plexus, and (8) internal carotid artery. The ascending palatine artery is in the anterior pillar. The descending palatine artery is in the posterior pillar. The tonsillar artery is in the posterior pillar as is also the pharyngeal artery. He advises that tonsillectomy should be deferred if inflammation is present, and cautions against pernicious anemia, leukemia, albuminuria and the menstrual period. Operation is contraindicated in hemophilia and purpura. The amount of hemorrhage at the time of operation depends on the skill of the operator. Ligature of the common carotid is not recommended but suture of the pillars is.

Baum [27] says that a clot should never be left in a bleeding tonsillar fossa. He prefers ether for anesthesia, the pharyngeal reflex being abolished but the laryngeal being retained. Novocain is a satisfactory local anesthetic, but cocain is dangerous and sloughing has followed the use of quinin and urea hydrochlorid. "There is no doubt that deaths have occurred from status lymphaticus." (Just as they formerly occurred from "heart failure"—in other words, from an unknown cause.) Acidosis often occurs but is not serious, as a rule. Sepsis occasionally occurs. Pulmonary abscess after tonsillectomy occurs in two different ways; by aspiration of blood and by infection through the circulation, either venous or lymphatic. (A septic thrombus forms in the venous plexus around the tonsil and the lung abscess results from an embolus detached from this thrombus.)

Dabney [28] reports four cases of delayed secondary hemorrhage occurring after tonsillectomy in the course of twelve years' work. One occurred ten days after tonsillectomy. Two patients were operated on under local anesthesia and two under general. The hemorrhage apparently was the result of separation of a slough.

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24. Ann. Otol., Rhinol. & Laryngol. **28**:337, 1919.
25. Ann. Otol., Rhinol. & Laryngol. **28**:344, 1919.
26. Texas State J. M. **14**:300 (Jan.) 1919.
27. Ann. Otol., Rhinol. & Laryngol. **28**:37, 1919.
28. Kentucky M. J. **17**:204 (May) 1919.

Lillie and Lyons [29] say that: (1) Tonsillectomy is justified in every frank case of myositis or arthritis; (2) a marked improvement occurs in 79 per cent. of such cases from tonsillectomy alone; (3) all dental sepsis should be removed, and (4) the size of the tonsil has no bearing on its possibilities for infection.

Albert and Douglass [30] state that bone or cartilage has been found in the tonsils in the following forms: (1) Elongation of hyoid or styloid process, and (2) bony plates or nodules or cartilaginous nodules.

LaMotte [31] reports a case of styloid process appearing in the throat along the left anterior pillar as a glistening surface that felt hard. The tonsils were removed and a piece of the process three-fourths of an inch long dissected out with great relief to the symptoms. (Such cases are apt to present great difficulties to the man who does tonsillectomies, unless he is sufficiently familiar with the literature to recognize the condition.)

Taylor [32] is convinced that septic tonsils and enlarged infected adenoids are an important factor in the etiology of recurrent vomiting; of twenty-one cases operated on, only one was unimproved after removal of tonsils and adenoids.

Milne [33] reports two cases of phlyctenular disease that cleared up promptly on removal of adenoids. He finds that over 80 per cent. of children with enlarged glands have adenoids.

Baum [34] states that in the bleeding of hemophiliacs after tonsil and adenoid operations, transfusion is the remedy of choice. Adenoid bleeding is scarcely serious. Otitis media may follow tonsil and adenoid operations. The same author finds that acidosis occurs more often after tonsil and adenoid operations than in any other one class of patients but that it is not serious as a rule. He advises pre-operative and postoperative examination of the urine for acetone and diacetic acid, with administration of sodium bicarbonate and glucose as measures of safety.

Bane [35] reports the case of a boy, aged 13, in whom a peritonsillar abscess was diagnosed, but on incision nothing was found. A gland was removed for diagnosis and the growth found to be a large cell sarcoma. Radium gave considerable temporary improvement, but the patient died a few weeks later.

Dean [36] believes that not only all tuberculous retropharyngeal abscesses, but all other abscesses should be opened externally. For

29. J. A. M. A. **72**:1214 (April 26) 1919.
30. Ann. Otol., Rhinol. & Laryngol. **26**:909, 1919.
31. Laryngoscope **29**:288, 1919.
32. Minnesota M. J. **2**:61 (Feb.) 1919.
33. Brit. J. Ophth. **3**:163, 1919.
34. Ann. Otol., Rhinol. & Laryngol. **28**:37, 1919.
35. Ann. Otol., Rhinol. & Laryngol. **28**:828, 1919.
36. Ann. Otol., Rhinol. & Laryngol. **28**:566, 1919.

this purpose he makes an incision just in front of the sternocleidomastoid muscle, with the lower end opposite the cricoid. The vascular sheath of the carotid is exposed and the finger inserted between the vascular sheath and the visceral fascia and passed down to the retropharyngeal space. The operation is simple, requires but a few minutes and should be almost without shock.

Brown [37] states that 96 per cent. of cases of acute retropharyngeal abscesses occur in children under 6 years of age, and 50 per cent. between the ages of 6 and 12 months.

Mosher [38] had a patient develop thrombosis of the internal jugular and pyemia as a result of retropharyngeal abscess.

Jewell [39] had a female patient, aged 13, with nasal voice, lumps in the throat and intermittent headache and earache. The growth which was attached to the left lateral and posterior wall of the postnasal space bled readily. The lymph glands on the left side of the neck were enlarged. Later, vomiting and blindness, first of the left eye and then of the right, developed, followed by coma and death. The growth was found to be endothelioma.

Ray [40] reports a case of sarcoma of the nasopharynx that was treated by radium. It improved at first but the patient died two months later.

White [41] observed a girl, aged 13, with a large fibroma of the nasopharynx.

Patterson [42] reports a case of fibroma of the nasopharynx in a boy, aged 18. Symptoms had been present for two years. They were: obstruction of the left naris, change in speech, pain in the left cheek, pain over the right eye, firm swelling in the temporal region, below the zygoma and in the nasopharynx.

Barroud [43] reports a case of complete bony atresia of both choanae in a baby aged 3 days. The symptoms were inability to drink and a profuse discharge from each nostril. He drilled a hole 4 mm. in diameter through each choana and passed a rubber tube into one hole and out of the other. The child now drinks freely with no disturbance of breathing and has increased considerably in weight.

St. Clair Thompson [44] reports the case of a female infant, aged 4 weeks, in whom there were three good sized vestibules to the nose with two columellae. The two external nostrils were true nostrils. The two false nostrils were culdesacs ¼ and ½ inch long.

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37. Laryngoscope **29**:638, 1919.
38. Laryngoscope **28**:638, 1919.
39. J. Laryngol., Rhinol. & Otol. **34**:306, 1919.
40. Laryngoscope **29**:602, 1919.
41. Laryngoscope **29**:499, 1919.
42. J. Laryngol., Rhinol. & Otol. **34**:306, 1919.
43. Arch. f. Ohren-Nasen- u. Kehlkopfh. **103**: (Abst.) 4, 1919.
44. J. Laryngol., Rhinol. & Otol. **34**:207, 1919.

Dean and Armstrong [45] found nasal sinus diseases as a cause of multiple arthritis in children. They also found sinus infection to blame for repeated colds after slight cause, for a case of noma, for cyclic vomiting, for asthenia, etc. Methods of diagnosis of accessory sinus disease in children are very unsatisfactory and great patience and persistence are necessary to arrive at definite conclusions. The most common symptoms were sneezing, recurrent stopping of the nose, frequent colds, nasal discharge, headache, poor appetite, poor color, etc. Direct examination of the nose was unsatisfactory. The nasopharyngoscope was a great help. Roentgen-ray examination is very necessary to determine the size of the sinuses, but not much help in learning their pathologic condition. Their treatment was first to remove adenoids and tonsils, and if this did not relieve the trouble to open the maxillary sinus in the lower meatus.

Albright [46] says there is no doubt that most cases of migraine are caused by accessory sinus disease.

Vail [47] reports four cases of orbital abscess due to intranasal suppuration. One patient had exophthalmos of the right eye and thrombosis of the cavernous sinus from sphenoidal suppuration. Another patient had exophthalmos from abscess of the posterior ethmoid cells. The globe was pushed straight forward. The third patient had abscess of the anterior ethmoids and the globe was pushed forward and toward the temple. The fourth patient had abscess of the frontal sinus. The globe was extruded to a less extent and was pushed downward. In all four cases the exophthalmos was on the right side. The first and third patients died. The second patient recovered. The fourth patient disappeared from view. Vail had six recoveries out of seven cases, before the days of modern ethmoid operations. In these he did external operations. One patient died from brain abscess. Six of these cases occurred in young adolescents who developed abscesses as a result of tonsillitis, measles and scarlet fever.

Wood [48] had a case of osteomyelitis of the frontal bone following frontal sinusitis. He considers such conditions as more common after acute frontal sinusitis than after the chronic form. (In my experience such conditions are more commonly the result of tertiary syphilis.)

Benian and Hayton [49] consider the causative organisms of ozena to be the *Bacillus capsulatus* of Lowenburg, the acid-fast bacillus of

45. Ann. Otol., Rhinol. & Laryngol. **28**:452, 1919.
46. Journal-Lancet **39**:490, 1919.
47. Laryngoscope **29**:263, 1919.
48. Laryngoscope **29**:612, 1919.
49. J. Laryngol., Rhinol. & Otol. **34**:325, 1919.

McKenzie and Wingrave and the cocco-bacillus of Perez. They apply glycerin or glucose to the nose, painting it from one to six times daily, and advise against douching.

Erzner,[50] reporting on vaccine and serum therapy of ozena, says: "It is most discouraging that this work should all be negative."

Unger [51] presented a case of leprosy where the first lesions were in the nasal mucosa, which showed three little tubercles. Diagnosis was confirmed by both sections and smears..

Rose [52] reports a case of round cell sarcoma of the antrum in a boy, aged 15. He has treated three such cases in children, one aged 4, one 12 and one 15. Shattuck in the discussion warns against errors of laboratory diagnosis in such cases.

LARYNX, TRACHEA, BRONCHI AND ESOPHAGUS

Albrecht [53] demonstrated sections of the larynx showing both tubercle bacilli and *Spirochaeta pallida.*

Denker [54] states that trauma of the larynx may result in death from hemorrhage, asphyxia or by mediastinal abscess. The larynx is protected from injury by its position under the chin, by its elasticity and by its movability.

Myers [55] reports a case of hoarseness due to paresis of the thyro-arytenoideus internus caused by suction used in treatment of the accessory sinuses.

Jackson [56] believes that closing the opening in the tracheotomy tube as far as possible without danger to the patient develops the laryngeal muscles and tends to prevent and to cure laryngeal stenosis.

Faulkner [57] reports a case with paralysis of the left vocal cord, associated with paresis of the sternocleidomastoid, trapezius, tongue, omohyoid and left arm. The lesion must have been in the cord, probably above the second and third cervical vertebrae.

White [58] observed a case of syphilitic laryngitis in a child of 7. The epiglottis was swollen and ulcerated, the swelling extending down into the larynx and hiding the cords.

Hill [59] advises radium in the treatment of papilloma of the larynx.

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50. Laryngoscope **29**:21, 1919.
51. Laryngoscope **29**:316, 1919.
52. Laryngoscope **29**:176, 1919.
53. Arch. f. Ohren-Nasen- u. Kehlkopfh. **103**: (Abst.) 24, 1919.
54. Laryngoscope **29**:60, 1919.
55. Laryngoscope **29**:720, 1919.
56. Laryngoscope **29**:16, 1919.
57. Laryngoscope **29**:60, 1919.
58. Laryngoscope **29**:500, 1919.
59. J. Laryngol., Rhinol. & Otol. **34**:250, 1919.

Grant [60] removed a papilloma of the larynx in a boy 4 years of age under suspension laryngoscopy.

Tod [61] had a patient, aged 4 years, die five weeks after tracheotomy and excision of a laryngeal papilloma. The postmortem examination showed false membrane in the larynx, trachea and bronchi. Purulent bronchitis was present. Smears gave streptococci and bacilli which did not resemble diphtheria.

Jackson [62] says that metallic foreign bodies, glass, pebbles and vulcanite cause very little reaction in the bronchi. Soft rubber is more irritating and vegetable substances, such as beans, peas, maize and peanuts, give a very violent reaction which is generally fatal if left alone. Roasted peanuts give the most violent reaction. Most foreign bodies tend to migrate downward towards the periphery. When the foreign body becomes fixed, a septic cavity results. Foreign bodies are more common in the right bronchus than in the left. In cases in which a foreign body has been retained a long time, clinical signs of tuberculosis result. In old cases the pus is very foul, dark and abundant. In peanut cases the pus is pink in color. Subglottic edema is apt to result in children under 19 months.

St. Clair Thompson [63] reports the case of a girl, aged 10, who had teeth extracted. Four weeks later a foreign body in the lung was suspected because of wheezing, cough, etc. Roentgen-ray examination showed a tooth in the lung. Direct bronchoscopy under chloroform was done for forty-five minutes without results. A month later, lower bronchoscopy was done under chloroform and was successful. Recovery was uneventful. He also reports a case of collar button in the right bronchus of a child, producing collapse of the lung of one year's duration. (I have had a collar button in the left bronchus two years.)

Rosier [64] reports a tooth plate in the trachea of a soldier for four months. He had received a wound and was operated on, under chloroform. On awakening he noticed the absence of a left upper tooth, but was told it had fallen on the floor and was lost. Three days later he was evacuated after being examined by the medecin major who found nothing but a few râles of bronchitis. Some months later he was gassed. He ate and slept perfectly, but three or four times during the day and night he had violent coughing spells. He was examined laryngoscopically and laryngitis was diagnosed. Four months after his first operation he was examined and a foreign body found in the trachea. Under cocain anesthesia it was removed. Prompt recovery followed.

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60. Ibid.
61. J. Laryngol., Rhinol. & Otol. **34**:254, 1919.
62. J. A. M. A. **73**:672 (Aug. 30) 1919.
63. J. Laryngol., Rhinol. & Otol. **34**:361, 1919.
64. Rev. de Laryngol., Otol. et Rhinol., (April 30), 1919.

Barthes [65] reports the removal of a live leech from the larynx.

St. Clair Thompson [66] uses his report of a tooth impacted in the bronchus as a text for giving the advantages of lower bronchoscopy over upper bronchoscopy, e. g.: (1) Less trouble with the anesthetic; (2) fewer assistants needed; (3) use of shorter bronchoscopic tube; (4) better illumination; (5) larger field of vision; (6) greater facility of manipulation; (7) less leverage on lung; (8) shorter time required; (9) more certain results, and (10) greater security should the foreign body change position.

Arrowsmith,[67] in an article on the history of bronchoscopy, gives abstracts of 140 cases of foreign bodies in the bronchi and lungs before the days of bronchoscopy.

Schmieglow [68] calls attention to the possibility of suffocation from rupture of tuberculous lymph glands into a bronchus and reports a case where he made a diagnosis of such a condition.

Guthrie [69] says that the blind removal of foreign bodies from the esophagus is scarcely to be defended. He reports the case of a poorly nourished baby that had inhaled a fishbone. Upper bronchoscopy failed. Tracheotomy was necessary the same evening on account of edema of the larynx. Lower bronchoscopy next day also failed. The child died two days later of bronchopneumonia.

Digestion of the esophagus is a cause of postoperative hemorrhage.

Pringle and Teacher [70] have had eighteen cases, most of them abdominal cases. Vomiting begins soon after operation. The vomitus is acid and scalds the throat. The amount of blood vomited is small. Postmortem, numerous submucous hemorrhages, erosions and perforations of the esophagus were found with fibrinous exudate on the pleura opposite the esophagus. The submucous hemorrhages showed that the condition existed antemortem.

Oppikofer [71] says that foam in the pyriform sinus is a symptom very suggestive of diverticulum of the esophagus.

Thompson [72] had a girl, aged 15, who had a fusiform dilatation of the esophagus which was covered with *Oidium albicans*. Lavage with hydrogen peroxid and eusol relieved but did not cure the condition.

Farren [73] found fibroma of the esophagus in a boy, aged 10.

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65. Rev. de Laryngol., Otol. et Rhinol. **40**:391, 1919.
66. Loc. cit.
67. Laryngoscope **29**:673, 1919.
68. Arch. f. Ohren-Nasen- u. Kehlkopfh. **103**: (Abst.) 65, 1919.
69. J. Laryngol., Rhinol. & Otol. **34**:38, 1919.
70. Brit. J. Surg. **6**:523, 1919.
71. Arch. f. Ohren-Nasen- u. Kehlkopfh. **103**: (Abst.) 62, 1919.
72. J. Laryngol., Rhinol. & Otol. **34**:101, 1919.
73. Arch. f. Ohren-Nasen-u. Kehlkopfh. **103**: (Abst.) 68, 1919.

Keiper [74] contributes an article on tight strictures of the esophagus due to burns. He recommends that no attempt be made at bougieing until two sets of roentgenograms have been made to locate accurately the site of the stricture. No bougies should be passed, except under direct inspection through the esophagoscope. Blind bougieing is dangerous. Frequent anesthesia for bougieing is highly dangerous. The strictures caused by lye are often multiple and tortuous.

MISCELLANEOUS

Lake,[75] in an article on aural bacteremia, considers it a condition in which living bacteria are present in the blood stream. It is to be distinguished from pyemia, in which there is only occasional entry of bacteria into the blood stream. The presence of bacteria is indicated by the temperature. Bacteria are found in greatest numbers during the time when the temperature is rising. They diminish in number when the temperature falls. "In those conditions in which they are constantly present the temperature never falls very low." Such cases, as well as the cases in which the temperature rises and falls excessively, are apt to end fatally. Rigors are not present in bacteremia. The temperature remains between 100 and 104 F. These seems to be cerebral stimulation, and the patient's mental processes are unusually quick. The prognosis is not bad. The treatment should be by: (1) autogenous vaccines; (2) blood antiseptics, such as hexamethylenamin in full doses, and (3) physiologic sodium chlorid solution subcutaneously.

Primary aural diphtheria has been seen in both sexes, according to Pugnat.[76] It attacks both adults and children, but is more common in children. It may appear before the nasal symptoms. Discharge from the ear should be examined bacteriologically.

Putawski [77] calls attention to dysphagia as a symptom of dilatation of the left ventricle.

Goldstein [78] concludes that epistaxis occurs as one of the earliest symptoms of "flu," that it seems to be invariably on the septal side of the naris and that cases in which epistaxis occurred were the most liable to develop complications. The *Streptococcus hemolyticus* was definitely established as the etiologic factor in the epistaxis. In sixty cases he used horse serum and had no fatalities.

Roy,[79] in an interesting article on syphilis among the blacks of Africa, dealing largely with the history of syphilis, mentions 135 cases in seventeen of which there were perforations of the septum, perfora-

74. Laryngoscope **29**:48, 1919.
75. J. Laryngol., Rhinol. & Otol. **34**:110, 1919.
76. Rev. de Laryngol., Rhinol. et Otol. **40**:377, 1919.
77. Arch. f. Ohren-Nasen- u. Kehlkopfh. **103**: (Abst.) 68, 1919.
78. Laryngoscope **29**:447, 1919.
79. Rev. de Laryngol., Otol. et Rhinol., (June 15), 1920.

tions of the palate in nine, perforations of both septum and palate in twelve, syphilitic osteitis in twenty, and syphilis of the larynx in two cases. No case of syphilis of the brain and spinal cord, or syphilis of the labyrinth or syphilitic paralysis of the larynx was seen.

Richardson [80] reports a case of condyloma of the anterior nares, an unusual manifestation of syphilis, that responded promptly to arsphenamin.

Mahler [81] reports a case of hereditary syphilis in a girl, aged 14, who had parenchymatous keratitis. Deafness developed suddenly and is complete in the right ear and severe in the left. Caloric and rotation nystagmus are absent. The fistula symptom was present.

Goeckerman, Barlow and Stockes [82] found shortened bone condition in 78 per cent. of cases of syphilis. The test has only a restricted value.

Peck's [83] experience is that chronic septic foci of the teeth and tonsils cause or contribute to thyroid disease. Operation should be done in all cases of exophthalmic goiter if removal of existing foci has not cured, providing there is not marked cardiac degeneration. A thyroid gland causing interference with respiration, speech, digestion, or a laryngeal cough, should receive early surgical attention. Many large goiters should be operated for cosmetic reasons. A hard nodular goiter in an elderly individual should be operated radically for it is probably malignant. Exophthalmos is apt to persist after thyroid resection and may demand an operation on the orbital walls.

Corwin,[84] in reporting a case of posticus paralysis resulting from a goiter operation, quotes Mayo to the effect that in possibly 10 per cent. of the goiter operations at the Mayo clinic some temporary hoarseness remains afterward, while in 3 per cent. there is permanent difficulty with one cord, or loss of voice. Mathews of the Mayo clinic found the vocal cords paretic in seventeen of 1,000 goiter operations.

80. Ann. Otol., Rhinol. & Laryngol. **28**:786, 1919.
81. Arch. f. Ohren-Nasen- u. Kehlkopfh. **103**: (Abst.) 42, 1919.
82. Am. J. Syphilis **3**:240 (April) 1919.
83. Ann. Otol., Rhinol. & Laryngol. **28**:781, 1919.